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MICROENCAPSULATION: A REVIEW

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ABSTRACT
Microencapsulation is the enveloping of core materials like liquid droplets or fine solid particles or sometimes gasses with a polymeric coating material to form microcapsule, having an average diameter as small as 1 µm to several hundred micrometers. For the coating of core materials sometimes fats and waxes are also used. The basic aim of microencapsulation is to protect the core material or API from the surrounding environment or to control its release. There are various methods for preparing microcapsules, but No single microencapsulation process is versatile to all core material candidate or item applications. The methods used are broadly classified into (i) physical methods: (a) physico-chemical (b) physico-mechanical and (ii) chemical methods. They can be evaluated for particle size, shape and surface morphology, bulk density, angle of repose, mass and coating thickness etc. Further, the microcapsules have specific release patterns and mechanisms at the time of use. Microencapsulation technology is of interest to a wide range of industries, including pharmaceutical, food, agriculture, biotechnology, cosmetic, petroleum and other industries with various significant advantages. The concept of packaging microscopic quantities of materials within microspheres dates back to the 1930s and since then it is advancing. A wide range of core materials has been encapsulated including adhesives, agrochemicals, live cells, active enzymes, flavors, fragrances, vitamins, water and pharmaceuticals. In this article brief information about the history, advantages, disadvantages, and applications, methods of preparation, evaluation and recent advances and applications of Microencapsulation technique is mentioned.

KEYWORDS: Angle of repose, API, Bulk density; coating and mass thickness, encapsulate, microcapsule, microspheres; particle size, shape and surface morphology.

1. INTRODUCTION
Microencapsulation involves the coating of particles ranging dimensionally from several tenths of a micron to 5000 microns in size or Microencapsulation is the enveloping of liquid droplets or fine solid particles to form microcapsule, having an average diameter as small as 1 µm to several hundred micrometers. Microencapsulation technology is of interest to a wide range of industries, including pharmaceutical, food, agriculture, biotechnology, cosmetic and other industries with various significant advantages, including: (i) An effective protection of the encapsulated active ingredient against degradation (ii) The possibility to control the release rate of the active ingredient.[1] Based on the diameter the encapsulated particles have different names.[2]

Table No. 1: Diameter and Type of particle.

Diameter	Type of particle
Less than 1 micron	Nanoparticle
3 to 800 micron	Microparticle
Larger than 1000 micron	Macroparticle

Micro-particles are the polymeric entities falling in the range of 1-1000 µm, covering two types of the forms, Microcapsules (micrometric reservoir systems) and Microspheres (micrometric matrix systems).[3] In a simplified way a microcapsule is a little circle with a uniform divider around it. The material inside the microcapsule is alluded to as the centre, inward stage, or fill, while the divider is infrequently called as shell, covering, or film.[4]

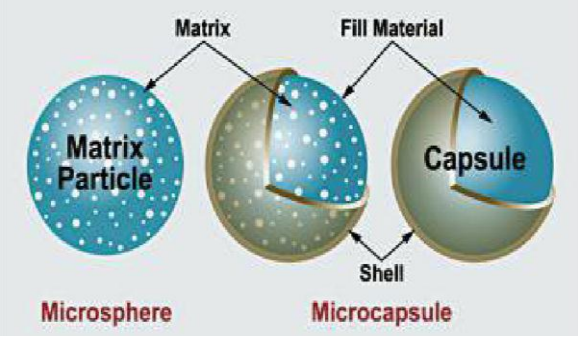

Figure No. 1: Microcapsule with core and shell.

2. HISTORY

The concept of packaging microscopic quantities of materials within microspheres dates back to the 1930s and the work of Bungenberg de Jong and co-workers on the entrapment of substances within coacervates.[5]

Microencapsulation of pharmaceuticals was first investigated in 1931 by preparing gelatin spheres using coacervation technique. Processes and materials used for coating have since been developed by the pharmaceutical industry to aid in formulation of various dosage forms such as tablets, capsules, injectibles, powders, and topical.[6]

In the early 1950s Barrett k. Green developed the microencapsulation that used the process of phase separation coacervation.[7] The first commercial application of encapsulation was by the National cash register company for the manufacture of carbonless copying paper in 1953.[8] On July 5, 1955, Dayton, Ohio, resident and National Cash Register Company employee Barrett K. Green received a patent for the process of microencapsulation.[9]

Advantages

- This procedure can be utilized for changing over fluid medications as a part of a free streaming powder.
- The medications, which are delicate to oxygen, dampness or light, can be settled by microencapsulation.
- Contrariness among the medications can be avoided by microencapsulation.
- Vaporization of numerous unstable medications e.g. methyl salicylate and peppermint oil can be avoided by microencapsulation.
- Many medications have been microencapsulated to diminish poisonous quality and GI bothering including ferrous sulphate and KCl.
- Adjustment in site of retention can likewise be accomplished by microencapsulation.
- Lethal chemicals, for example, bug sprays might be microencapsulated to decrease the likelihood of sharpening of factorial individual.[10]

Disadvantages

- No single microencapsulation process is versatile to all core material candidate or item applications.
- Complicated process and requires talented work to oversee.
- Incomplete or intermittent covering.
- Non reproducible and insecure discharge attributes of coated products.
- Inadequate stability or time span of usability of touchy pharmaceuticals.
- Economic limitations.[11]

3. Reasons for Microencapsulation

- The essential purpose behind microencapsulation is observed to be either for supported or delayed medication discharge.
- This system has been generally utilized for covering taste and scent of many medications to enhance tolerant consistence.
- This strategy can be utilized for changing over fluid medications as a part of a free streaming powder.
- The medications, which are touchy to oxygen, dampness or light, can be settled by microencapsulation.
- Incongruence among the medications can be anticipated by microencapsulation.
- Vaporization of numerous unpredictable medications e.g. methyl salicylate and peppermint oil can be anticipated by microencapsulation.
- Many medications have been microencapsulated to diminish poisonous quality and GI disturbance including ferrous sulphate and KCl.
- Change in site of assimilation can likewise be accomplished by microencapsulation.
- Dangerous chemicals, for example, bug sprays might be microencapsulated to diminish the likelihood of sharpening of factorial individual.[12]

4. Materials Involved

The material present inside the microcapsule is referred to as the core, internal phase, or fill, whereas the wall is sometimes called a shell, coating, or membrane. Some materials like lipids and polymers, such as alginate, may be used as a mixture to trap the material of interest inside. Most microcapsules have pores with diameters between a few micrometers and a few millimetres.[13]

Core Materials: The core material, characterized as the particular material to be covered, can be fluid or strong in nature. The organization of the centre material can be differed, as the fluid centre can incorporate scattered and additionally disintegrated materials. The strong centre is dynamic constituents, stabilizers, diluents, excipients, and discharge rate retardants or quickening agents. The capacity to fluctuate the centre material structure gives clear adaptability and use of these qualities regularly permits solid outline and improvement of the wanted microcapsule properties.[14]

Coating Materials: The choice of fitting covering material chooses the physical and substance properties of the resultant microcapsules/microspheres. While selecting a polymer the item necessities i.e. Adjustment, diminished instability, discharge attributes, natural conditions, and so forth ought to be thought about. The polymer ought to be equipped for framing a film that is firm with the centre material. It ought to be artificially perfect, non-responsive with the centre material and give the fancied covering properties, for example, quality, adaptability, impermeability, optical properties and solidness.

Examples

- **Water soluble resins:** Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxymethylcellulose, Hydroxy ethylcellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.

- **Water insoluble resins**: Ethylcellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (Ethylene Vinyl acetate), cellulose nitrate, Silicones, Poly lactideco glycolide.

- **Waxes and lipids**: Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates.

- **Enteric resins**: Shellac, Cellulose acetate phthalate, Zein.

Properties of coating materials

➢ Adjustment of core material.
➢ Idle toward dynamic fixings.
➢ Controlled discharge under particular conditions.
➢ Film-shaping, malleable, bland, stable.
➢ Non-hygroscopic, no high consistency, efficient.
➢ Dissolvable in a fluid media or dissolvable, or liquefying.
➢ The covering can be adaptable, weak, hard, thin and so forth.[15]

5. Morphology and Types of Microcapsules

The morphology of microcapsules depends mainly on the core material and the deposition process of the shell. Microcapsules may have regular or irregular shapes and, on the basis of their morphology, can be classified as mononuclear or continuous core/shell microcapsule, multinuclear or polynuclear microcapsule, and matrix microcapsule.

Mononuclear or continuous core/shell microcapsules have a spherical geometry with a continuous core region surrounded by a continuous shell. Multinuclear or polynuclear microcapsules have an irregular geometry and contain a number of small droplets or particles of core material. In matrix microcapsule, the core material is distributed homogeneously into the shell material. The term microcapsule is usually preferred if the entrapped substance is completely surrounded by a distinct capsule shell and the term matrix microcapsules or the microspheres are used if the entrapped substances is dispersed throughout the microsphere matrix. In addition to these three basic morphologies, microcapsules can also be dual core and multilayer microcapsule with single core or they may form cluster of microcapsules.[16]

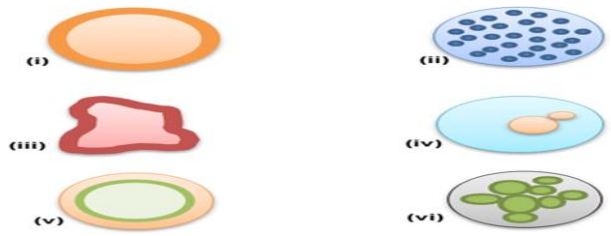

Figure No. 2: Different types of microcapsules: (i) simple microcapsule, (ii) matrix (microsphere), (iii) irregular microcapsule, (iv) multicore microcapsule, (v) multiwall microcapsule, and (vi) assembly of microcapsule.

Table No. 2: Terminology of microencapsulation products.[9]

Terminology of microencapsulation products

Terminology	Description	Size range	Schematic illustration
Microcapsules (narrow sense of Meaning	Products of coating liquid nuclei with solid walls.	μ m	
Nanocapsules	Same structure as microcapsules, but smaller.	nm	
Microspheres or Microparticles	The cores and walls are both solid. Often, there is no clear distinction between them: the thick solid wall functions as a porous matrix where active substances are embedded.	μm	
Nanospheres or Nanoparticles	Same structure as microspheres, but smaller.	nm	

6. Criteria for The Preparation of Micro-Spheres

Preparation of microspheres ought to fulfil certain criteria

1. The ability to incorporate reasonably high concentrations of the drug
2. Stability of the preparation after synthesis with a clinically acceptable shelf life.
3. Controlled particle size and dispersability in aqueous vehicles for dispersions.
4. Release of active reagent with a good control over a wide time scale.
5. Biocompatibility with a controllable biodegradability and
6. Susceptibility to concoction alteration.[17]

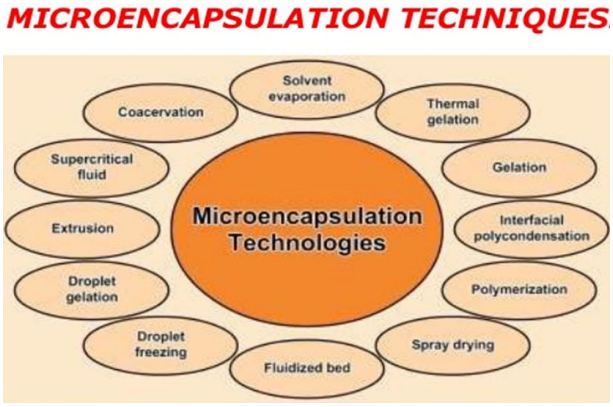

Figure No. 3: Microencapsulation techniques.

7. **Microencapsulation Methods**

Physical Methods

Physico-chemical

✓ Coacervation
✓ Solvent evaporation, solvent extraction
✓ Layer-by-layer adsorption
✓ Complex precipitation
✓ Ionic gelation
✓ Supercritical fluid precipitation

Physico-mechanical
✓ Air suspension
✓ Spray drying
✓ Pan coating
✓ Extrusion
✓ Electrostatic encapsulation
✓ Vacuum encapsulation
✓ Multi orifice centrifugal
Chemical methods
✓ Polymerization, In-situ emulsion, suspension, Dispersion
✓ Interfacial polycondensation.[18]

(Methods not currently applicable to pharmaceutical preparations are vacuum deposition and polymerization techniques).[19]

Physical methods
Air suspension: Microencapsulation via air suspension procedure comprise of the scattering of strong, particulate centre materials in a supporting air stream and the shower covering reporting in real time suspended particles. Inside the covering chamber, particles are suspended on an upward moving air stream. The plan of the chamber and its working parameters impact a recycling stream of the particles through the covering zone bit of the chamber, where a covering material, generally a polymer arrangement, is shower connected to the moving particles. Amid every go through the covering zone, the centre material gets an addition of covering material.

The cyclic procedure is rehashed, maybe a few hundred times amid handling, contingent upon the motivation behind microencapsulation the covering thickness desired or whether the core material particles are thoroughly encapsulated. The supporting air stream also serves to dry the product while it is being encapsulated. Drying rates are directly related to the volume temperature of the supporting air stream.[20]

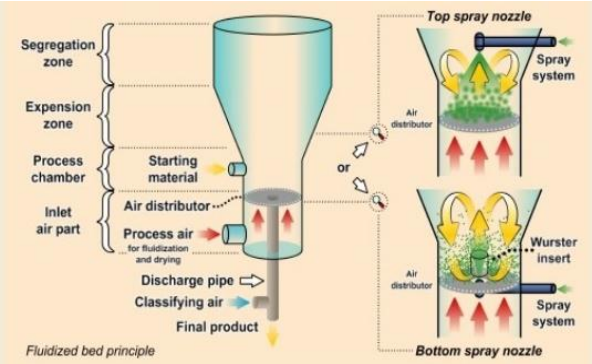

Figure No. 4: Air Suspension Technique.

Application of air suspension
• Colette and Rubin depicted covering of headache medicine gems of different work sizes with blends of ethyl cellulose and methylcellulose showered from ethylene chloride: isopropyl alcohol (1: 1) solution utilizing Wurster air suspension mechanical assembly.

• Caldwell and Rosen utilized an air suspension coater to successfully apply dexamphetamine sulphate onto sugar pellets utilizing arrangement of gelatine as a part of hydroalcholic dissolvable as adhesive. At that point covered with different materials, including beeswax glyceryl monostearate and distearate to get lipid coated microcapsules with supported discharge properties.

Coacervation Phase Separation
Coacervation is a colloid marvel. In the event that one begins with an answer of a colloid in a fitting dissolvable, then as indicated by the way of the colloid, different changes can achieve a decrease of the solvency of the colloid. As an after effect of this diminishment a substantial part of the colloid can be isolated out into another stage. The first one stage framework gets to be two stages. One is rich and the other is poor in colloid fixation. The colloid-rich stage in a scattered state shows up as indistinct fluid beads called coacervate drops. After standing these blend into one clear homogenous colloid-rich fluid layer, known as the coacervate layer which can be kept in order to deliver the divider material of the resultant containers.

This procedure of microencapsulation is by and large alluded to The National Cash Register (NCR) Corporation and the licenses of B.K. Green.[20]

This procedure comprises of three Steps
• Formation of three immiscible stages; a fluid assembling stage, a centre material stage and a covering material stage
• Deposition of the fluid polymer covering on the centre material
• Rigidizing of the covering material

Step-1: The initial step of Coacervation stage partition includes the development of three immiscible substance stages: a fluid vehicle stage, a covering material stage and a centre material stage. The three stages are framed by scattering the centre material in an answer of covering polymer; the vehicle stage is utilized as a dissolvable for polymer. The covering material stage comprises of a polymer in a fluid stage, is framed by utilizing one of the of stage detachment coacervation strategy, i.e. by changing the temperature of the polymer arrangement, by including an answer, or by inciting a polymer-polymer association.

Step-2: It includes the testimony of the fluid polymer covering upon the centre material. This is finished by controlled blending of fluid covering material and the centre material in the assembling vehicle. The fluid covering polymer saved on the centre material if the polymer is adsorbed at the interface shaped between the centre material and fluid stage. The diminishment in the aggregate free interfacial vitality of the framework

advance the affidavit of the covering material, brought by the lessening of the covering material surface region amid blend of the fluid polymer beads.

Step-3: In the last stride rigidizing of the covering material done by the warm, cross connecting desolvation procedures, to frames a self-supporting microcapsule.[20]

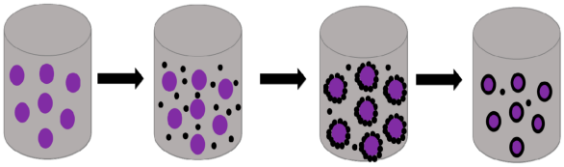

Figure No. 5: Coacervation Process.

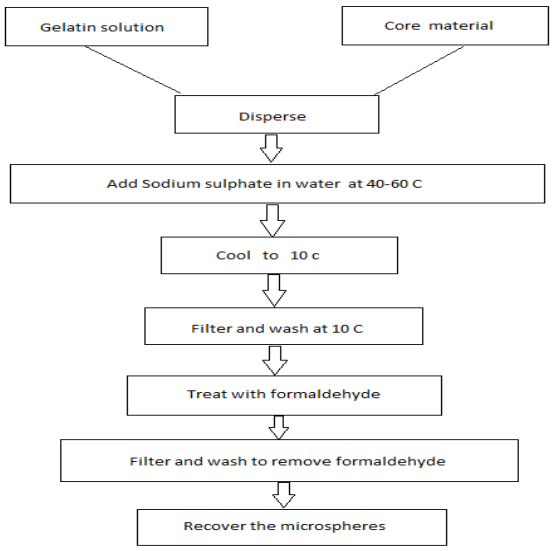

Figure No. 6 Simple Coacervation Process.[21]

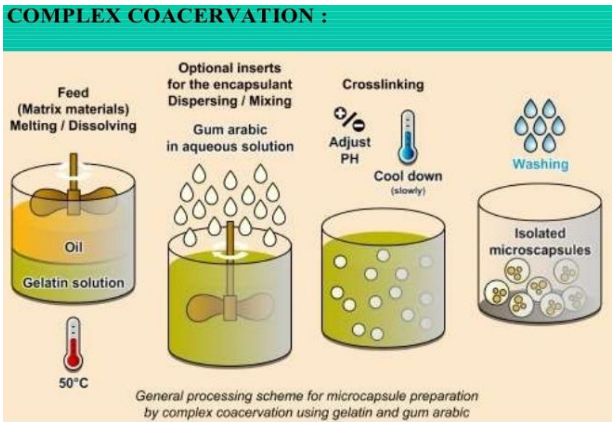

Figure No. 7: Complex Coacervation Process.

Centrifugal extrusion: Liquids are typified utilizing a pivoting expulsion head containing concentric spouts. In this procedure, a fly of centre fluid is encompassed by a sheath of divider arrangement or dissolve. As the stream travels through the air it breaks, attributable to Rayleigh unsteadiness, into beads of centre, each covered with the divider arrangement. While the beads are in flight, a liquid divider might be solidified or a dissolvable might be vanished from the divider arrangement. Since the vast majority of the beads are inside ± 10% of the mean width, they arrive in a restricted ring around the splash spout. Henceforth, if necessary, the containers can be solidified after arrangement by getting them in a ring-formed solidifying shower. This procedure is great for framing particles 400–2,000 µm (16-79 mils) in distance across. Since the drops are framed by the separation of a fluid fly, the procedure is appropriate for fluid or slurry. A high creation rate can be accomplished, i.e., up to 22.5 kg (50 lb) of microcapsules can be delivered per spout every hour per head. Heads containing 16 spouts are accessible.[22]

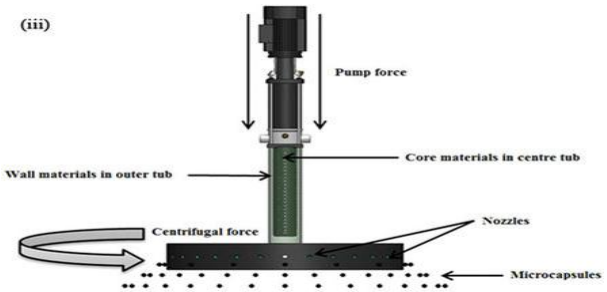

Figure No. 8: Extrusion process.

Advantages

- They don't require any numbers, or many moving parts.
- This makes them simple to create with a wide range of materials.
- It likewise permits them to move at high speeds with insignificant upkeep.
- Their yield is relentless and reliable.
- The vast majority of all, they are little contrasted with different sorts of pumps that make a similar yield.

Disadvantages

- They utilize turn rather than suction to move water, and in this manner have no suction control.
- This implies a diffusive pump must be put submerged, or prepared, before it will move water.

Pan Coating: The Pan Coating process, broadly utilized as a part of the pharmaceutical business, is among the most seasoned modern methods for framing little, covered particles or tablets. The particles are tumbled in a dish or other gadget while the covering material is connected gradually. The dish covering process, generally utilized as a part of the pharmaceutical business, is among the most established mechanical methods for shaping little, covered particles or tablets. The particles are tumbled in a skillet or other gadget while the covering material is connected gradually regarding microencapsulation, strong particles more noteworthy than 600 microns in size are for the most part viewed as fundamental for viable covering, and the procedure has been widely utilized for the readiness of controlled – discharge dots. Medicaments are normally covered onto different round substrates, for example,

quintessence sugar seeds, and after that covered with defensive layers of different polymers. In practice, the covering is connected as an answer, or as an atomized shower, to the craved strong core material in the covering dish. More often than not, to evacuate the covering dissolvable, warm air is disregarded the covered materials as the coatings are being connected in the covering skillet. At times, last dissolvable evacuation is proficient in a drying stove.[23]

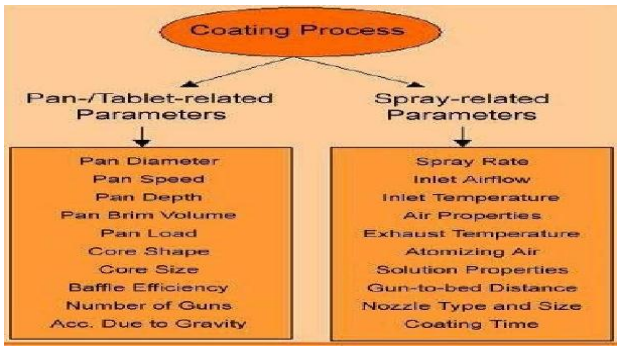

Figure No. 9: Representation of typical Pan Coating.

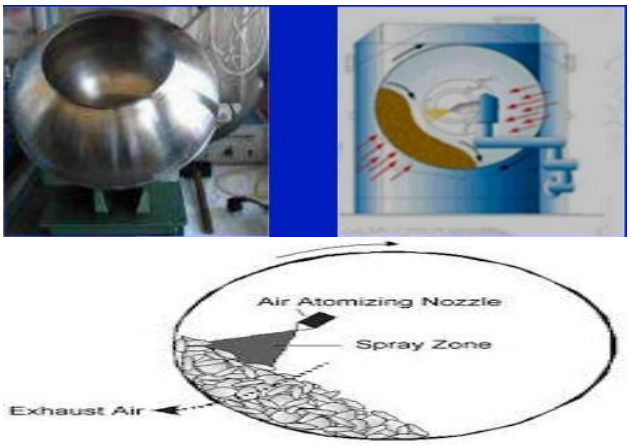

Figure No. 10: List of variables affecting pan coating.

Advantages

1. It is used for coating the core material by using pans
2. It is used for solid particles for coating.

Disadvantages

1. It is an expensive process.
2. It requires skill persons

Application of Pan coating:

- Lowy 14 skillets covered adjusted granules containing nitro glycerine with different cellulose subsidiaries, for example, methylcellulose, ethyl cellulose, or cellulose acetic acid derivation utilizing beeswax or castor oil as a plasticizer.

- Rosen and Swintoskey 15 reported pan covering of trimeperazine that contain taking after step:

1. 35S-marked trimeperazine tartrate, a hostile to pruritic agent mixed with powdered starch and sugar
2. This is a plied on sugar pellet utilizing hydroalcholic gelatin adhesive as a part of covering pan.
3. Dried, screened and after that covered with arrangement of 11%w/w glyceryl monostearate, 11% w/w glyceryl monostearate & 3% w/w white beeswax in CCl_4, come about microcapsules demonstrated managed discharge in human subjects after oral organization.

Spray–drying: It serves as a microencapsulation system when a dynamic material is broken down or suspended in a dissolve or polymer arrangement and gets to be caught in the dried molecule. The primary focal points is the capacity to handle labile materials in view of the short contact time in the dryer, moreover, the operation is prudent. In present day splash dryers the consistency of the answers for be showered can be as high as 300 m Pas.

Spray drying and spray congealing procedures are comparable in that both include scattering the centre material in a melted covering substance and showering or bringing the centre covering blend into some natural condition, whereby, generally quick cementing (and arrangement) of the covering is influenced. The chief contrast between the two strategies is the methods by which covering hardening is proficient. Covering cementing on account of splash drying is affected by quick vanishing of a dissolvable in which the covering material is broken up. Covering hardening in splash coagulating techniques, in any case, is expert by thermally hardening a liquid covering material or by setting a broke down covering by presenting the covering - centre material blend into a non-dissolvable. Expulsion of the non-dissolvable or dissolvable from the covered item is then expert by sorption, extraction, or dissipation strategies.

Microencapsulation by spray drying is directed by scattering a centre material in a covering arrangement, in which the covering substance is broken down and in which the centre material is insoluble, and afterward by atomizing the blend into air stream.[24]

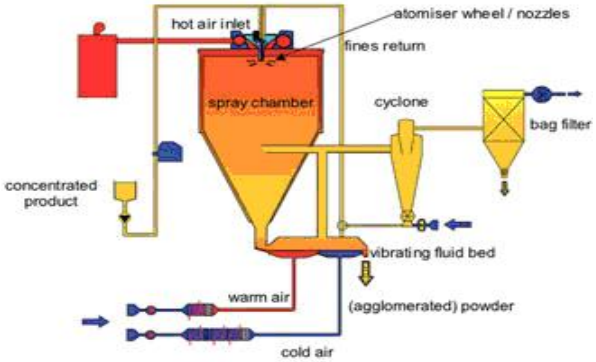

Figure No. 11: Spray dryer.

Advantages

- Quick, single stage operation, can be utilized for warmth sensitive substance.

Disadvantages

- Permeable covering, not appropriate for taste and smell veiling and for controlled discharge formulation, high cost of creation.

Applications of spray drying

- Marottaetal in patent doled out to National Starch and Chemical Corp speech, utilized a fluid arrangement of corrosive esterdextrins to exemplify emulsified scattering lemon oil by spray drying.

- Sager, inpatent appointed to Beecham Group ltd., Great Britain, depicted shower drying of penicillin as takes after

1. For instance of process, high moved ampicillin trihydrate suspended in weaken arrangement of sodium carboxy methylcellulose.
2. Control of frothing by expansion of ethanol
3. Filtration
4. Shower dried at 160^0 C and outlet temperature is 84^0 C
5. Item under 75 micron are reused
5. Item under 75 micron are reused

Application of Spray congealing:

- Robinson and Swintosky microencapsulated particles of sulfaethylthiadiazole by blending them with molten hydrogenated castor oil at 110 ^{0}C; then suspension was spray congealed into air cooled chamber utilizing radiating wheel atomizer.

- Koffdis parsed thiamine monohydrate into a liquid mixture of mono-and diglycerides of palmitic and stearic corrosive at 74^0C splash solidified into encompassing air at 20^0C. Normal particle size is around 60 micron and the procedure was accounted for to be suitable for the embodiment of vitamin of B gathering for tasking reasons

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 in which centre material is broken down in the covering polymer arrangement, a lattice - sort microcapsule is framed. When all the dissolvable for the polymer is dissipated, the fluid vehicle temperature is decreased to encompassing temperature (if required) with proceeded with unsettling. At this stage, the microcapsules can be utilized as a part of suspension frame, covered on to substrates or segregated as powders.

The dissolvable dissipation system to deliver microcapsules is appropriate to a wide assortment of fluid and strong centre materials. The centre materials might be either water solvent or water insoluble materials. An assortment of film shaping polymers can be utilized as coatings. Illustration: Evaluation of sucrose esters as option surfactants in microencapsulation of proteins by the dissolvable dissipation technique.[25]

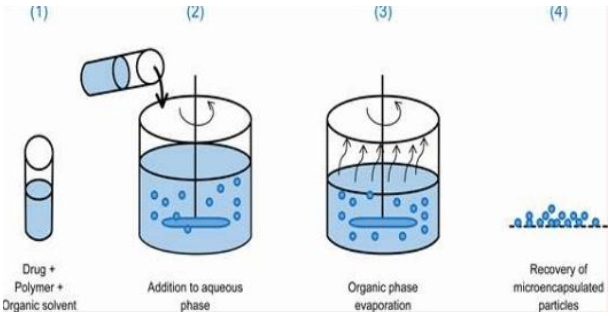

Figure No. 12: Solvent evaporation process.

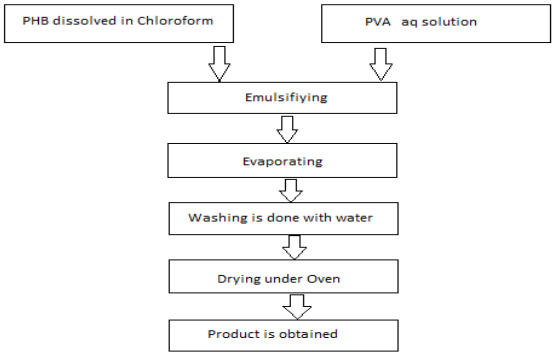

Figure No. 13: Solvent evaporation steps.

Advantages

1. It is used for both small scale and large scale industries.
2. Its construction is simple and it is operated easily.
3. It requires low maintenance.

Disadvantages

1. Its heat economy is less.
2. It is not suitable for heat sensitive materials.

3. When concentration is increased heat transfer rate drastically decreases.

Chemical Methods

Polymerization: In this procedure the case shell will be shaped at or on the surface of the bead or molecule by polymerization of the responsive monomers. The substances utilized are multifunctional monomers. For the most part utilized monomers incorporate multi-functional isocyanates and multifunctional corrosive chlorides. These will be utilized either independently or as a part of blend. The multifunctional monomer broke up in fluid centre material and it will be scattered in watery stage containing scattering specialist. A co reactant multifunctional amine will be added to the blend. This out comes in quick polymerization at interface and era of container shell happens. A poly urea shell will be framed when isocyanate responds with amine; polynylon or polyamide shell will be shaped when corrosive chloride responds with amine. At the point when isocyanate responds with hydroxyl containing monomer produces polyurethane shell. Like IFP the case shell development happens in light of polymerization monomers added to the exemplification reactor. In this procedure no responsive operators are added to the centre material, polymerization happens solely in the persistent stage and on the constant stage side of the interface shaped by the scattered centre material and consistent stage. At first a low sub-atomic weight prepolymer will be framed, over the long haul the prepolymer develops in size, it stores on the surface of the scattered centre material there by creating strong case shell. Case: embodiment of different water immiscible fluids with shells shaped by the response at acidic pH of urea with formaldehyde in watery media.[26]

Interfacial polymerization: In Interfacial polymerization, the two reactants in a polycondensation meet at an interface and respond quickly. The premise of this technique is the traditional Schotten Baumann response between a corrosive chloride and a compound containing a dynamic hydrogen iota, for example, an amine or liquor, polyesters, polyurea, polyurethane. Under the correct conditions, thin adaptable dividers frame quickly at the interface. An answer of the pesticide and a diacid chloride are emulsified in water and a watery arrangement containing an amine and a polyfunctional isocyanate is included. Base is available to kill the corrosive shaped amid the response. Consolidated polymer dividers shape immediately at the interface of the emulsion beads.[27]

In-situ polymerization: In a couple microencapsulation forms, the immediate polymerization of a solitary monomer is done on the molecule surface. In one process, E.g. Cellulose filaments are epitomized in polyethylene while inundated in dry toluene. Regular testimony rates are around 0.5µm/min. Covering thickness ranges 0.2-75µm. The covering is uniform, even over sharp projections.[28]

Table No: 03 Comparision between Interfacial polymerization and In-situ polymerization.[29]

Interfacial polymerization	In-situ polymerization
1.The multifunctional monomer broke down in fluid core material which will be then scattered in water stage containing scattering operator. 2.A co reactant multifunctional amine will be added to the blend 3.This in fast polymerization at interface and era of container shell happens 4.Polynylon or polyamide shell will be shaped when corrosive chloride responds with amine A polyurea shell will be shaped when isocyanides responds with amine	1.In this procedure no receptive specialists are added to the core material 2.Polymerisation happens only in the continuous stage and on the continuous stage side of the interface framed by the scattered core material and continuous stage 3.At first a low atomic weight prepolymer will be framed, over the long haul the prepolymer develops in size 4.It stores on the surface of the scattered core material accordingly creating strong container shell.

8. RELEASE METHODS AND PATTERNS

Even when the aim of a microencapsulation application is the isolation of the core from its surrounding, the wall must be ruptured at the time of use. Many walls are ruptured easily by pressure or shear stress, as in the case of breaking dye particles during writing to form a copy. Capsule contents may be released by melting the wall, or dissolving it under particular conditions, as in the case of an enteric drug coating. In other systems, the wall is broken by solvent action, enzyme attack, chemical reaction, hydrolysis, or slow disintegration. Microencapsulation can be used to slow the release of a drug into the body. This may permit one controlled release dose to substitute for several doses of non-encapsulated drug and also may decrease toxic side effects for some drugs by preventing high initial concentrations in the blood. There is usually a certain desired release pattern. In some cases, it is zero-order, i.e. the release rate is constant. In this case, the microcapsules deliver a fixed amount of drug per minute or hour during the period of their effectiveness. This can occur as long as a solid reservoir or dissolving drug is maintained in the microcapsule. A more typical release pattern is first-order in which the rate decreases exponentially with time until the drug source is exhausted. In this situation, a fixed amount of drug is in solution inside the microcapsule. The concentration difference between the inside and the outside of the capsule decreases continually as the drug diffuses. Nevertheless, there are some other mechanisms that may take place in the liberation of the encapsulated material. These include biodegradation, osmotic pressure, diffusion, etc. Each one will depend on the composition of the capsule made and the environment it is in.

Therefore, the liberation of the material may be affected by various mechanisms that act simultaneously.[30]

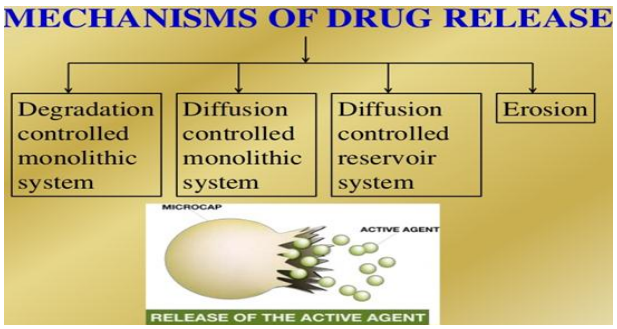

Figure No. 14: Mechanisms of Drug Release From Microcap.

9. Applications

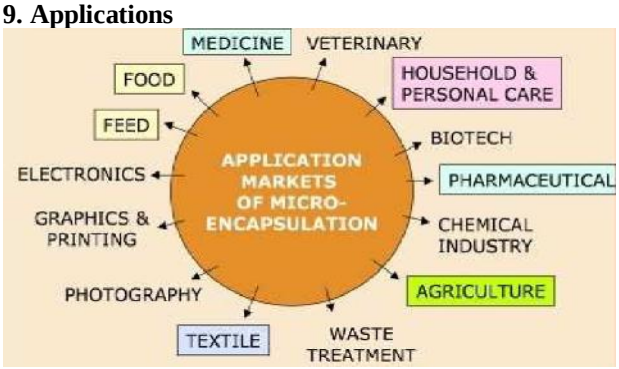

Figure No.15 Application Markets.

Pharmaceutics: One of the significant applications zones of epitome method is pharmaceutical/ biomedical for controlled/maintained medication conveyance. Potential uses of this medication conveyance framework are substitution of helpful operators (not taken orally today like insulin), quality treatment and being used of immunizations for treating AIDS, tumours, growth and diabetes. Protein, for example, insulin, development hormone and erythropoietin (used to treat pallor) are case of medications that would profit by this new type of oral conveyance.[31]

Microencapsulation frames minor fluid filled, biodegradable small scale inflatable's containing different medication arrangements that can give better medication conveyance and new restorative medicines for strong tumours and safe contaminations. Microcapsules containing antitumor medicines and visualization markers, the treatment can be guided ideal to the tumour, which has a few advantages over systemic treatment, for example, chemotherapy. The microcapsule additionally contain a difference operator that empowers C-T, X-beam or ultrasound imaging to screen the dispersion inside the tissues to guarantee that the whole tumour is dealt with when the microcapsules. Microencapsulation electrostatic handling framework 2 test, or MEPS-2,led by Dennis Morrison at NASA Johnson space centre, was performed on the station in 2002 and included inventive epitome of a few distinctive against malignancy drugs, magnetic activating particles and embodiment of hereditarily engineered DNA.

with more than 60years of exemplification innovative work understanding, southwest research institute(SwRI) is the field and have aptitude in various specialized fields, for example, pharmaceuticals, sustenance and nutrition, polymer and material science and process designing, SwRIs epitome masters take care of item stability, release and application issues in an extensive variety of businesses. SwRI has led more than 1,000 embodiment investigate programs for business and government customers.[31]

There are many reasons why tranquilizes and related chemicals have been microencapsulated. The innovation has been utilized generally as a part of the outline of controlled discharge and maintained discharge dose shapes.[32]

- To cover the intense taste of medications like Paracetamol, Nitrofurantoin and so forth. Many medications have been microencapsulated to diminish gastric and other G.I. tract aggravations. Supported discharge Aspirin arrangements have been accounted for to bring about fundamentally less G.I. seeping than customary arrangements.
- A fluid can be changed over to a pseudo-strong for simple taking care of and capacity. eg. Eprazinone.
- Hygroscopic properties of centre materials might be decreased by microencapsulation eg. Sodium chloride.
- Carbon tetra chlorides and various different substances have been microencapsulated to lessen their scent and instability.
- Microencapsulation has been utilized to give insurance to the center materials against climatic impacts, e.g. vitamin A palmitate.
- Separation of contradictory substance has been accomplished by epitome.
- Cell immobilization: In plant cell societies, Human tissue is transformed into bio-fake organs, in constant maturation forms.
- Beverage generation.
- Protection of particles from different mixes.
- Drug conveyance: Controlled discharge conveyance frameworks.
- Quality and security in nourishment, rural and natural divisions.
- Soil immunization.
- In materials: method for granting wraps up. Protection of fluid precious stones.[32]

10. EVALUATION

i. Particle size distribution: Particle size analysis of the microcapsules is done by sieve analysis method using Indian Standard Sieves i.e., 16, 20, 30, 40, 60 and #80. The amount retained on various sieves is weighed. From the obtained data, weight percent and average size can be calculated.[33]

Figure No. 16: Standard sieve.

ii. Shape and surface morphology: The shape and surface morphology of the microcapsules is considered by utilizing checking electron magnifying instrument. Microcapsules are mounted straight forwardly onto the Scanning Electron Microscope test stub utilizing two fold sided staying tape and is covered with gold film i.e., thickness 200 nm under lessened weight i.e., 0.001 mm of Hg.[34]

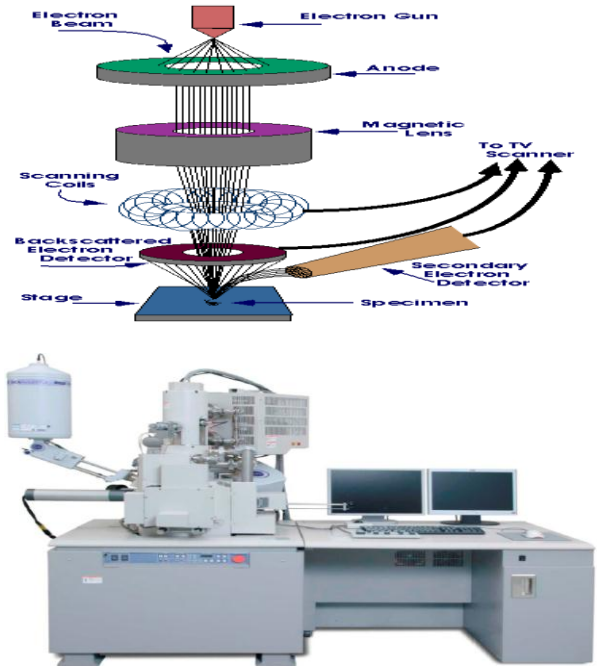

Figure No. 17: Scanning electron microscope.

iii. Carr's Index & Hausner's Ratio: The static point of rest was measured by settled pipe and detached cone strategy. The mass thickness of the blended microcapsules was computed in deciding the Hausner's proportion and Carr's file from the pored and tapped mass densities of a known weight of the example utilizing a measuring barrel.[35] The accompanying equations were utilized for ascertaining Carr's record: Carr's Index = [Tapped Density-Bulk Density/Tapped Density] ×100.

The Hausner proportion of the microcapsules fabricated utilizing diverse definitions was registered by taking after relationship: HR=ρT/ρB
Where, ρT is tapped density and ρB is bulk density.

iv. Bulk density: Accurately weighed microcapsules (Wm) were moved into a 100ml graduated barrel to get the clear volumes (V) of somewhere around 50 and 100 ml. The mass thickness was figured in gram per milliliter by the accompanying equation:
Bulk Density (ρρ) = [Weight of Microcapsules (g) (M) /Bulk Volume (ml) (V)]
Whereas, M = mass of the powder, Vo = volume of the powder

Figure No. 18: Bulk density Apparatus.

v. Angle of repose: A pipe was settled on and remains in such a way that the highest point of the pipe was at a stature of 6cm from the surface. The microcapsules were passed from the channel so they shape a heap. The tallness and the span of the load were measured and the point of rest was figured utilizing the condition[36]**;** Tan θ= h/r

Where h is the height of the heap and r is the radius of the heap.

Figure No. 19: Angle of repose.

vi. Thickness of coating: Thickness of aceclofenac microcapsules can be determined by using method of Luu. et. al using equation.[37]
h = r (1-p) d1 / 3[pd2 + (1-p) d1]

Whereas: h = wall thickness of microcapsules,
r = arithmetic mean radius,
d1 = density of core material,
d2 = density of coating material,
p = proportion of medicament in microcapsules.

vii. Practical yield: It is calculated by using the formula: % yield = weight of the microcapsules/ Theoretical weight of drug and polymer ×100

viii. Atomic force microscopy

It is a digital instrument used to study the surface morphology of the microspheres.[38]

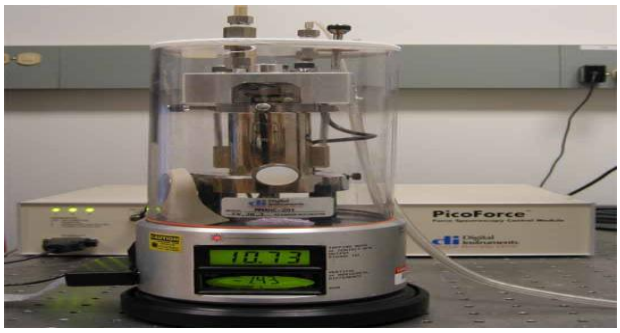

Figure No. 20 Atomic Force microscope.

11. RECENT ADVANCEMENTS

Since the carbonless copying paper was developed in 1954, the microencapsulation technology has been constantly improved, modified and adapted for a variety of purposes and uses. A wide range of core materials has been encapsulated including adhesives, agrochemicals, live cells, active enzymes, flavours, fragrances, vitamins, water and pharmaceuticals. Most capsule shell or coating materials are usually organic polymers but fats and waxes are also used.

- A number of pharmaceutical microencapsulated products are currently on the market such as aspirin, theophylline and its derivatives, vitamins, pancrelipase, anti hypertensive, KCl, progesterone and contraceptive hormone combinations.[39]

- Use of microparticle systems is not limited to the sustained or local delivery and has a wide range of applications. A limited number of examples are introduced below.

- Since it was first noticed that bio erodible hydrophobic polyanhydrides (example, poly (fumeric-co-sebacic anhydride)) exhibited strong bioadhesiveness, micro particles made of these polymers have been investigated as potential oral drug delivery systems. The bio adhesiveness in this case comes from the hydrogen bonding interaction between mucin and carboxylic acid groups that form during the polymer erosion.

- Furthermore, the small size of microparticles provides additional advantages by promoting cellular uptake of the formulation. Taking advantage of both the small size of microparticles and the chemical attributes of the polymeric system. The bio adhesive microparticles have shown enhanced oral bioavailabilty of dicoumarol, insulin and DNA.

- Polymeric microspheres have been used for delivery of DNA vaccines, which enable prolonged immune responses through sustained release of DNA. Encoding a protein antigen. It has been known that <10 µm particles are preferentially internalised through phagocytosis by macrophages and antigen presenting cells. Poly (lactic-co-glycolic acid) was used as an uncapsulating polymer in the initial research with promising results.

- On the other hand, disadvantages of PLGA particles in delivering DNA vaccines with acidification of microenvironment, which can inactivate encapsulated DNA, and slow release rate, which does not catch up with the life span of the target cells such as dendritic cells.

- In order to provide for rapid and turnable release and to avoid internal acidification, use was recently made of PH-triggered biodegradable polymers based on poly (orthoesters) and poly beta amino esters. These microparticles loaded with DNA were successfully internalised into the antigen presenting cells, enhanced immune response, and suppressed invivo tumour challenges significantly.[40]

- Microcapsules have also been applied in oil field additives, which were expected to create high economic value in the petroleum industry in recent years.

- Researchers actively explored the application of microencapsulated cell transplantation and microencapsulated drugs in the treatment of diabetes, Parkinson's disease, liver failure, tumor, etc. In self-healing materials, Kim prepared a water-treatment membrane that could restore its water flux and particle rejection properties autonomously. To achieve self-healing, a polyurethane shell acts as a protective coating and also controls the release of the isophorone diisocyanate core.

- In the food industry, microencapsulation of probiotic bacteria, which can be used to enhance viability during processing and are also utilized for targeted delivery in the gastrointestinal tract, has achieved remarkable benefits.

- Additionally, methods adopted from immobilized cell technology were applied for the microencapsulation of probiotics, often optimized towards specific requirements associated with the protection of probiotic cells in food production.

- In the cosmetics industry, to improve the stability or bioavailability of products, this tiny structure is commonly used to avoid incompatibility of substances, reduce odour of active ingredients, and for the protection of effective chemicals prone to oxidation or reaction, for example, vitamins, sun filters, moisturizers, fragrances, can be kept in chemical inert nylon microspheres.[41]

- Encapsulation technology recently took a giant leap forward as Balchem introduced the first product using a revolutionary encapsulation process. This new technology allows us to significantly increase the

concentration of the active ingredient in our encapsulated products.

- Balchem's SHURE Technology is based on a proprietary microencapsulation process that provides targeted nutrient delivery to the small intestine of ruminants. In simple terms, the microencapsulate is a substrate coated with another material to form a granule. In this case, a nutrient is coated with Balchem's proprietary lipid-based materials, all of which are GRAS and approved for use as a feed additive.

- The process is superior to other microencapsulation techniques in providing excellent barrier properties to water and microbes. This translates to excellent DURABILITY/STABILITY in the feed and PROTECTION in the rumen. In addition, through Balchem's proprietary.

- lipid-based coating technology, the microencapsulates are designed to be STABLE even after freeze and thawing allowing nutrients to escape the rumen and absorbed in the small intestine resulting in exceptional

BIOAVAILABILITY

- Micrographs taken of Balchem's SHURE Technology coating compared to competitor technology are shown in Figure 21 and demonstrate the consistency of Balchem's coating process. The new encapsulation process is more cost-efficient, allowing Balchem to provide a more concentrated level of nutrients, at a lower cost. As the first in an expected series of new products, New AminoShure-L will significantly lower costs. As part of the commitment to precision feeding advancements and to the dairy industry, Balchem's innovations will be realized as savings for the dairy producer.[42]

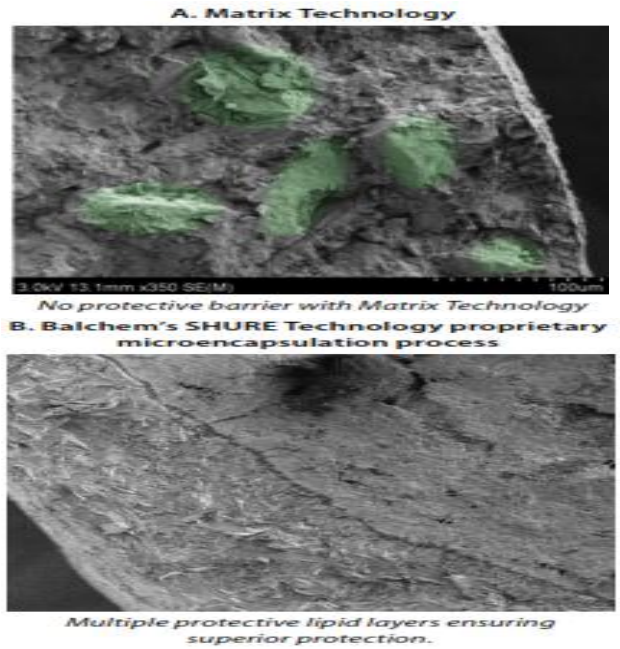

Figure No. 21: Comparision between Matrix and Balchem's SHURE Technology.

- In recent years, there has been an increasing interest in the use of natural antimicrobials in food products. An ongoing challenge with natural antimicrobials is their degradation during food storage and/or processing, which reduces their antimicrobial activity.

- Microencapsulation of natural antimicrobial compounds is a promising alternative once this technique consists of producing Microparticle, which protect the encapsulated active substances.[43]

- Microencapsulation is a promising technique to stabilize functional foods but the best technique for each functional food still remains a challenge.[44]

- Latest advancements in evaluating microcapsules is the X-ray computed tomography (XCT) Recently, this technology showed a wondrous ability in evaluating complex or porous systems, and it provides characteristic parameters to form a real system via a related procedure utilized XCT to observe the status and fracture behavior of microcapsules inside a cement paste matrix, and then elaborated 3D reconstructed tomographic images of the cement matrix with the assistance of 3D rendering based on the segmentation and data from XCT. Novel measurements, such as XCT, surely make it more intuitive to explore the internal structure of materials, and will notably be more conductive for its further development.[45]

CONCLUSION

Microencapsulation means packaging an active ingredient inside a capsule ranging in size from one micron to several hundred micrometers. The capsule protects the active ingredient from its surrounding environment until an appropriate time. Then, the material escapes through the capsule wall by various means, including rupture, dissolution, melting or diffusion. Microencapsulation is both an art and a science. The microencapsulation technique offers a variety of opportunities such as protection and masking, reduced dissolution rate, facilitation of handling, and spatial targeting of the active ingredient. For a good microencapsulation trained and experienced professionals are required. This approach facilitates accurate delivery of small quantities of potent drugs. By combining various other approaches, microencapsulation technique is finding a vital place in novel drug delivery system. It has a wide range of applications and is continuously being advanced according to the need in pharmaceutical field as well as in other markets. New processes are being developed using microencapsulation technique to avoid various problems.

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