A Review On MICROENCAPSULATION TECCHNIQUE

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Abstract

Microencapsulation can be described as heavy, fluid or gaseous substance packaging engineering with thin polymeric coatings, creating small particles called microcapsules. Microencapsulation is very helpful to increase the solubility of drugs. For the drugs of BCS Class-II we use this techniques which enables us to get more solubility and increase dissolution profile. This is the novel method of drug delivery. In future aspect we can use this technique in food industry, beverages. Microencapsulation approach for the preparation of an intrauterine contraception system was also suggested. This technique is helpful to overcome poor solubility, low Bioavaibility and less stability. This method also give more control over the drawback of conventional dosages form.

Keywords: Microencapsulation; Bioavaibility; Solubility; Novel Drug Delivery.

MICROENCAPSULATION

DEFINITION

It is defined as a system which covers solid particles, liquid droplets or gas bubbles, known as core material, with polymer or co-polymer materials called shell product.

HISTORY

Inventor: - Green, Barry Year: - 1950s

In the late 1930s, Barry Green, a research chemist at Dayton's National Cash Register Company, began to explore how the principle of microencapsulation could possibly be used in copying documents. If dye specks could be covered with a special fusible coating that would form a microcapsule, the use of ink could be much less messy and more effective. The possibilities of regulating the release of an active ingredient by encapsulating it had long fascinated scientists. Microencapsulation was fairly straightforward in theory; in fact,It was extremely difficult to get the right conditions. Green's invention would become the cornerstone of the software that creates documents from copiers and printers. Microencapsulation is essential to many other developments

today, including pesticides and pharmaceuticals that have been released over time. (Takka, S.et.al ;1999)

Until xerography, a clerk often used multipage forms interlaced with carbon paper to make copies of a file. Such packages were somewhat messy because users had to remove the carbon-paper pages and then dump them. It was often a struggle to read the last copy in a row. In 1942, Green had developed a working method for Lowell Schleicher Microencapsulating ink and carbon-free paper model. He collaborated with Thomas Busch of Appleton Coated Paper in Appleton, Wisconsin, on the difficult process of applying microcapsules to paper in a thin, porous layer over the next twelve years.

The material had three layers: the paper; a film of microcapsulated acid-sensitive dye; and a sheet of acid clay to transform the dye from translucent to dark blue or black. Pressure from a writing tool broke the dye microcapsules on each sheet's underside (except the last one); when the dye was released, it reacted on the next sheet's surface with the acid layer. Significant effort was made to model capsule walls that were adequately durable to survive storage but would crack under a pencil stress. Green used gelatin, a substance composed of long chains of chemically bound amino acids, to harden the cell walls. Once gelatin is handled with a reactive chemicals such as formaldehyde, glutaraldehyde, or tannic acid, the chains form new chemical relations. The effect is a three-dimensional network called a cross-linked gelatin that is thicker and less elastic than normal gelatin, resulting in a stronger and more stable microcapsule. Dye was dissolved in a fast-boiling organic solvent in order to make the microcapsules, and the resultant mixture was mixed at high speed in the presence of gelatin and gum arabic in liquid. With the launch of the groundbreaking Xerox 914, the development work ended in 1959. While being bulky and requiring constant attention, this computer made it possible to create faithful copies of practically any document for the first time without resorting to messy wet processes.(Prasanna,et.al;2010)

INTRODUCTION

Microencapsulation is characterized in a dormant shell is a system of encasing covering micron extend strong particles or beads of fluid or gasses, which as a result concentrate and jam them from the outside world. (Silva, P. T. D.,et.al;2014)

It is classified as microparticles, microcapsules or microspheres when the particle size is below 1 mm as nanoparticles, nano-capsules, nanospheres, and particles with a diameter of 3–800 mm. Particles in excess of 1000 mm are classified as macroparticles. (Wen, J., et.al;2014)

There are two elements of microparticles or microcapsules, namely base layer and cover or shield content. Core content requires an active ingredient when coating or securing the core material is the paint or hell material. Different substances such as active drug additives, hormones, peptides, reactive fats, meat products, pigments, paints, etc. may be embedded with various kinds of covering or shell materials such as ethylcellulose (EC), (HPMC), (Na CMC), (PLGA), polyester, chitosan, etc. (Iwamoto, S., et.al;2016).)

MICROENCAPSULATION CAN BE PERFORMED FOR

1. To shield fragile materials from the outside world.
2. Masking the organoleptic characteristics of the material such as color, taste, odor.
3. Product material controlled release.
4. Safely handling of toxic substances.
5. Medicines targeted release can be achieved.
6. To reduce harmful drug effects such as abdominal discomfort, e.g. aspirin medication helps to eliminate irritation in the abdominal region.

FORMULATION DIMENSIONS OF MICROENCAPSULATION 1) Capsules

It can usually be categorized as macrocapsules (> 5,000μm), microcapsules (0.2 to 5,000μm) and nanocapsules (<0.2μm) according to their volume. It can be classified into two classes in terms of form and construction: microcapsules and microspheres. (Wen, J., Chen, et.al;2014)

Microencapsules are the molecules that comprise of an inside core, predominantly central, comprising the API protected by a sheet of polymer which forms the membrane of the capsule. It is possible to distinguish between mononuclear and polynuclear microcapsules whether the heart is separated. (Silva, P. T. D.,et.al;2014)On the other hand, microsphere is a matrix framework in which the core of a polymer network is scattered and/or uniformly dissolved.

2) Materials of the Wall

Divider materials are basic to pick appropriately in light of the fact that they influence the proficiency and soundness of the microcapsule. The perfect dividers ought to have: the non-receptive nature of the center; the capacity to screen and hold the center inside the case; the possibility for the core to be maximized for protection from adverse conditions; the absence of an uncomfortable taste for food applicability and economic viability. Most walls have not all the required characteristics; it is common practice to mix more than one substance. These products are picked from a various sources of polymers i.e natural and synthetic, some of them are:

- **carbohydrates**: sugar, refined starch, dextrins, sucrose, cellulose and chitosan; gums: arabic gum, alginate and carrageenan;
- **lipids**: gelatin, paraffin, monoglycerides and diglycerides, hydrogenated oils and fats;
- **inorganic substances**: calcium sulfate and silicates; proteins: carbon, paraffin and diglycerides; Hydrogenated oils and fats;
- **inorganic materials**: sulfate for calcium and silicates; sugar, casein, gelatin and albumin proteins.
- (Nakagawa, K., et.al ;2004)

3) Core release in a Controlled manner

It should allow separates the core material from outside environment until it is required to be released. Release is most vital property at the right time and place in the encapsulation phase, increasing performance, reducing the necessary dosage of additives and extending the use of interesting compounds. The major factors influencing the released levels are the connections between the substance of the wall and the heart. In addition, certain factors affect the launch, such as core instability, core-wall content proportion, particle volume, and wall surface viscosity level. Diffusion, oxidation, solvent usage, pH, temperature and pressure are the key processes involved in the central launch. A variation of more than one process is being used in action. Diffusion happens in particular when the wall of the microcapsule is unchanged; releasing frequency are controlled with the core material and wall material's chemical properties also with some of the wall's physical properties. For example, during a process stage, certain acids can be released but covered something else. In some situations, certain preservatives are available on the material surface. Nonetheless, it is needed to control their distribution to other sections. (Rocha-Selmi,et.al ;2013)

Degradation release happens as protease and lipase enzymes, respectively, destroy proteins or lipids. An instance is a 50 percent reduction in the time required to mature cheddar cheese relative to the traditional maturing process. (Gu, J., Yang, X.,et.al ;2016)

Changes in Temperature will stimulate release of the core. The two distinct concepts are: heat-sensitive release, used for substances that extend or crumble when a crucial temperature reaching, and also activated fusion release causing wall surface melt and the reason is the increased in temperature. The example stated is cheese taste in the microwave popcorn due to fat encapsulation, resulting in a standardized taste distributed: when temperature rises to 57-90 ° C, the flavor is released.Pressure release happens when the capsule surface is squeezed, such as removing certain tastes through chewing gum chewing. (Casanova, F., et.al;2016)

CHOICE OF PROCESS OF MICROENCAPSULATION

1. The core type.
2. Microcapsule use purpose.
3. Particle dimensions required.
4. The heart and the wall's physical and chemical properties.
5. Needed the release mechanism.
6. The size of the production and the price.

(Markl, D et.al ;2015)

TYPES OF MICROENCAPSULATION ARE

1. Physico-chemical types a) Coacervation

b) Sol gel microencapsulation

c) Supercritical C02 microcapsulation supported

2. Chemical methods

a) polymerization of the interfaces

b) polymerization in situ

c) polymerization

3. Physical-mechanical processes

a) spraying and congealing

a) liquid bed coating

b) sheet coating

c) evaporation of solvents

1) Physicochemical Techniques:-

i) Coacervation and phase separation

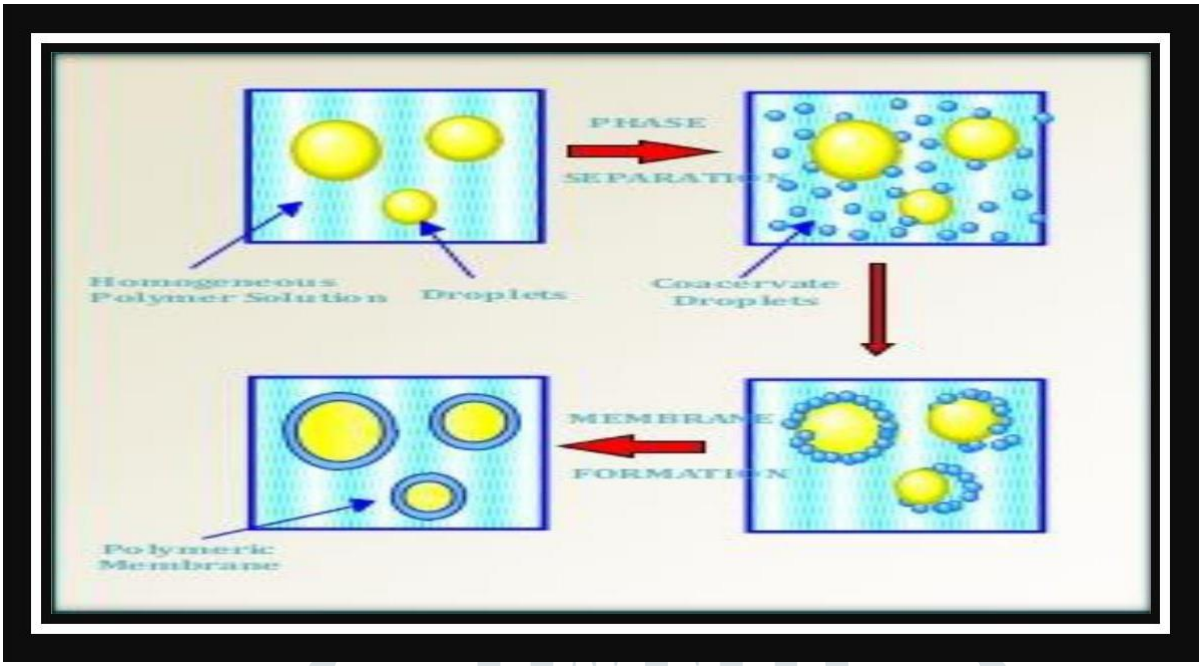
Coacervation is the procedure involving polymer deposition around the center by modifying the medium's physicochemical properties, such as medium temperature, ionic strength, pH and polarity. The basic coacervation technique is that in which there is single macromolecule, whereas it referred to as complicated coacervation when the opposing charges exist for two or more molecules. (Akyuz, L.,et.al 2017)

Coacervation process is easier, economical and don't require elevated temperatures or solvents of organic nature. Usually this technique helps to cover flavoured oils. One of the coacervation's main drawbacks is that it exists only within small levels of pH, concentrations of colloids and/or concentrations of electrolytes. (Weiβ, G.,et.al;1995)

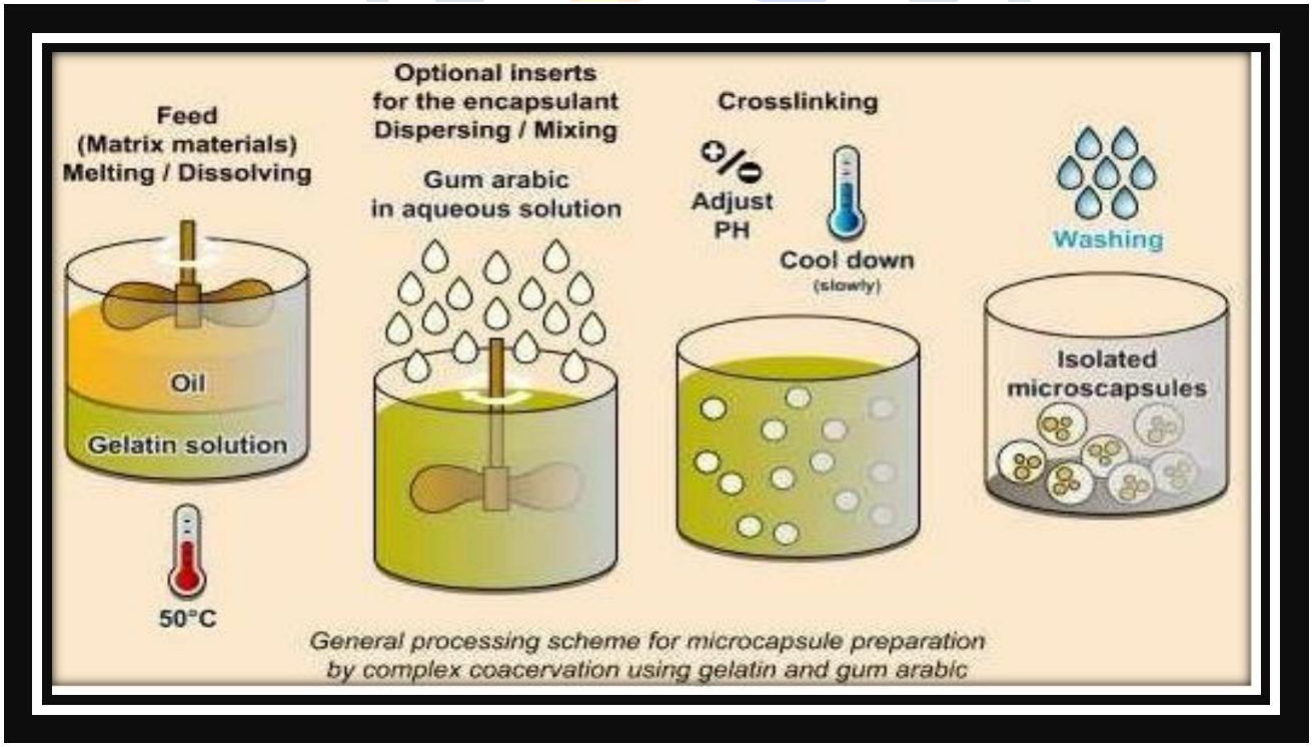
Examples:-

- Sweet orange oil covering with soy protein.
- Micro embedded B. L. and lactis. Acidophilus can better resist the in process product from stomach and intestine region liquids/juices by coacervation with coating material like pectin and casein.
- Co-capsulated aspartame, enhancing protection even at 80 degree celsius.

Simple Coacervation



➢ **Compex coacervation**



B) Supercritical fluids quickly expand to encapsulate polymer

Highly compressed gasses like Supercritical fluids are containing various favorable liquid and gas properties. Super-critical carbon dioxide, alkanes (Carbon no. 2 to Carbon no. 4) and nitrous oxide are the most commonly utilized. A slight variation in temperature or stress induces a significant modification in super-critical liquid volume at the critical point. Apart from its non- toxicand non-flammable qualities, supercritical carbon dioxide is commonly help during low value of critical temperature.; and it's commonly available, with high purity and in economical range.

The commonly employed approaches for these are

i) Supercritical approach quickly expansion.

The fluids are of supercritical type comprising the API and coat material content is stored at elevated pressure in this process, and then discharged by a narrow nozzle at atmospheric pressure. The sudden drop in stress allows the shell content to be desolved and then dispersed on the API creating a coating material film. The downside of this method is that in supercritical fluids, both the API and the coating material content must be strongly solublise. For addition, there are very few small stable energy density polymers (e.g. polydimethylsiloxanes (PDMS), polymethacrylates (PMA)). In that fluids including carbondioxide soluble. Use co-solvents can will enhance the solubilization of polymer in solvent. Non-solvents have application in some cases; this helps to enhance the solubilization in fluids of supercritical nature, but at atmospheric pressure it is difficult to dissolve the material of the shell. Previously, RESS microencapsulation of TiO2 nanoparticles utilizing ethanol as a polymer shell non-solvent such as polyethyleneglycol (PEG),(methyl methacrylate) were carried out. (de Farias,et.al;2018)

ii) Application of Gas Anti-Solvent (GAS) PROCESS

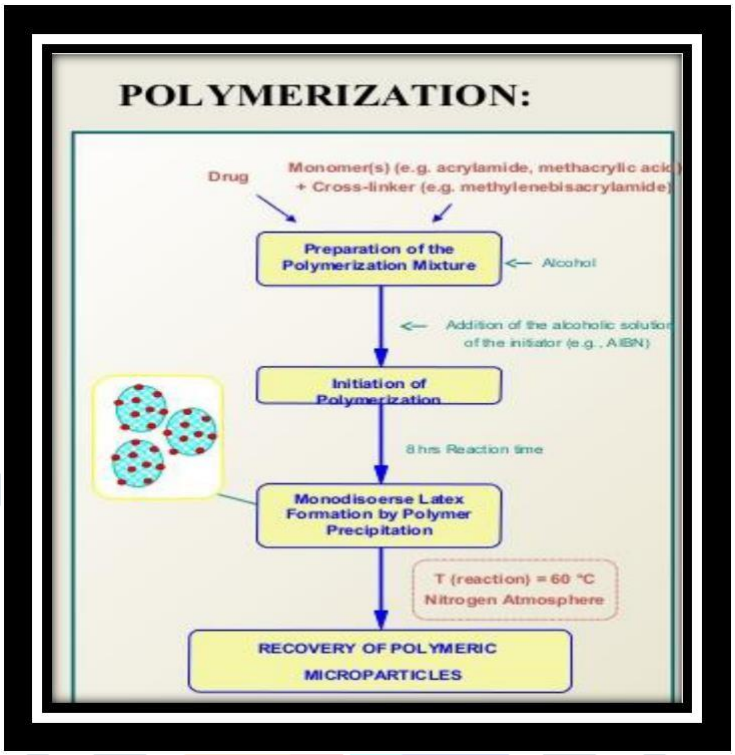
Anti-solvent supercritical fluid (SAS) is related to this method only. In that situation, supercritical fluid is applied to a shell substance solution and the API and held at too much high pressure (which is one of the requirements of method). Its leading to a solvent size increase which induces super saturation and allows the solute to precipitate. The solution must therefore be solublized in the water, but it should not be diluted in the oil and supercritical fluid combination. But, with the supercritical fluid, the liquid solution should be soluble with each other. This system is not fit for water-soluble component encapsulation, since liquid has poor solubility in supercritical fluids. Particles of submicron range can be produced by using this method.

iii) Gas-Saturated Solution Particles (GSSP)

This method is done by combining core and shell components with high-pressure supercritical fluid. Supercritical liquid enters the shell material during this procedure, causing expanding. The polymer

liquifies when the solution is warmed above the level of the glass phase. The shell content can be accumulated on the active ingredient after removing the stress. The center and shell materials in the super-critical liquid may not be soluble in this phase.

2) Chemical methods



a) Polymerisation

Types

i. Interfacial polymerization (IFP)

Multifunctional isocyanates and multifunctional acid chlorides are widely found monomers. It will be used in tandem or separately. The monomer which are multifunctional will solubilized in core material of liquid nature and then dispersed it in water phase with the agent i.e. dispersing. A multifunctional co-reactant amine is applied to the mixture. It results in accelerated surface polymerization and capsule shell production occurs. If isocyanate interacts with amine, polynylon, or polyamide shell if acid chloride reacts with amine, a polyurea shell will be formed. This creates a polyurethane layer as isocyanate reacts with monomer-containing hydroxyl. For example, using an interfacial polymerization process, encapsulated diammonium hydrogen phosphate by polyurethane urea membrane. An elevated synthesis yield (22 percent) of a microencapsule powder form production with a content filled of 62 wt percent of DAHP as calculated by the elementary examination. DAHP microcapsules average size is 13.35 mm. In addition, Ninety-five percent of the molecules are less than 30.1 mm in diameter.

ii. In situ polymerization

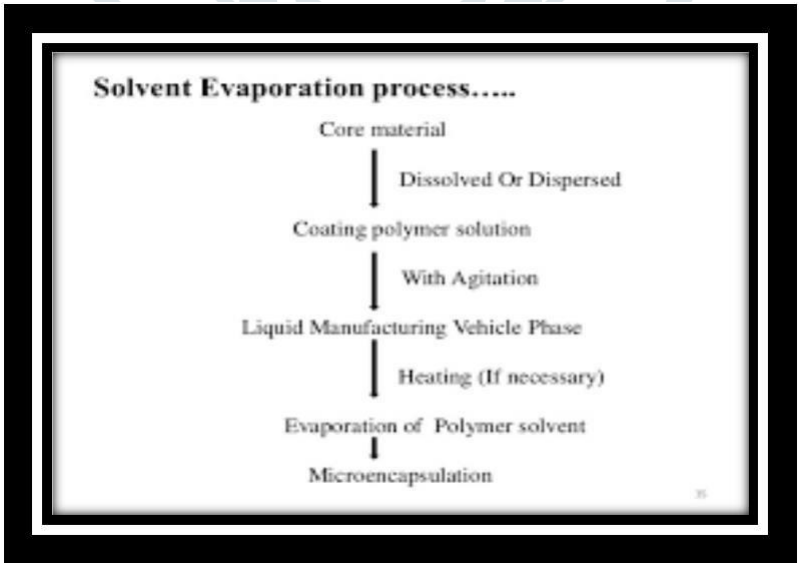
Because of polymerization activity of monomers applied to the embodiment framework, there container shell shaping happens like IFP. Receptive specialists are not applied profoundly in this framework, polymerization happens exclusively in the stage which is nonstop in framework and on these stage side of the interface made by the diffuse center and ceaseless stage in the framework. In the beginning, a pre polymer having small molecular weight of is produced by producing a strong shell of capsule (e.g. capsulation of many lipophilic liquids, with shell material created with the chemical reaction at conditions of acidic pH of urea, with formaldehyde reagent in water means prepared with carboxy-functionalized magnetic microcontrollers). The prepolymer can develop as time goes by.

(Mishra, M. et.al;2015)

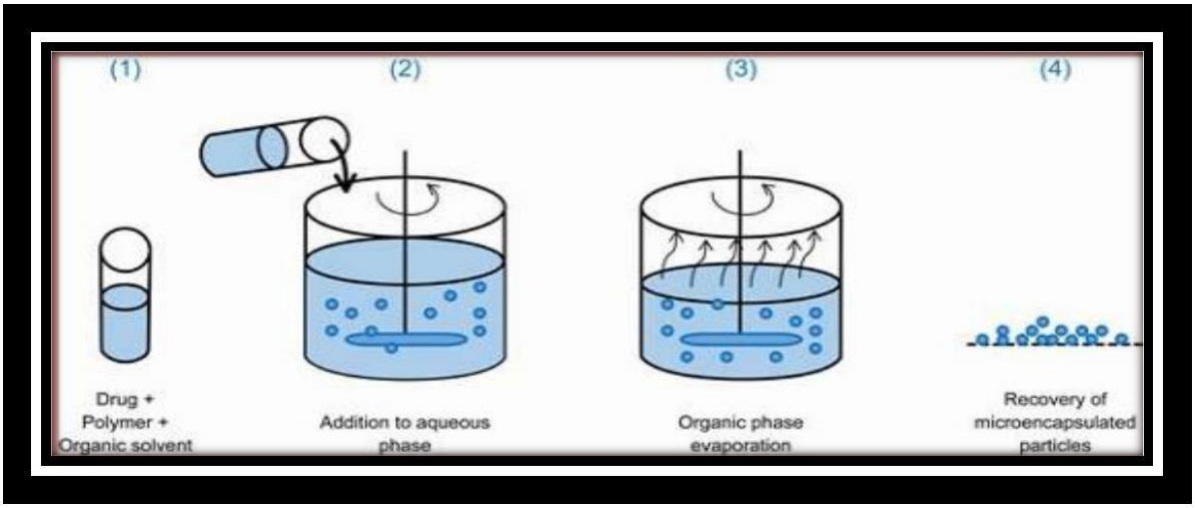
(b) Solvent evaporation

The method of solvent evaporation microencapsulation is commonly practiced in the pharmaceutical industry for the controlled release of narcotics. The polymer microspheres obtained with inside trapped material will gradually degrade and release the encapsulated product with a specific release profile. (Saffari, M., et.al;2016)

Process:-



Diagrammatic representation of solvent evaporation:-



Physical-mechanical methods

(a) Spray drying

The sumac taste was effectively microencapsulated by spray drying method in Nacl in salt taste cookies, salad and crackers microencapsulated oleoresin cardamom by spray drying method in gum arabica, malto dextrin and altered starch, resulting in increased oleoresin safety. Optimized probiotic microencapsulation of raspberry juice by 91.15 percent spray drying. The encapsulation of lipids through spray drying in potato starches, tapioca and maize has been efficient, with no conflicts between the materials encapsulated and wall.

B**) Spray cooling / congealing**

Spray microencapsulation is focused on cold air injection to allow particle solidification. Microparticles are formed from a solution of droplets comprising the substance of the base and surface. The atomizer nebulizes the solution and reaches a cavity in which low temperature air streams. The temperature drop results in the solidification of the product in the building, causing the substance to be encapsulated. It results in accelerated surface polymerization and capsule shell production occurs. If isocyanate interacts with amine, polynylon, or polyamide shell if acid chloride reaction take place with amine, a polyurea shell on to the core material will be formed.This creates a polyurethane layer as isocyanate reacts with monomer-containing hydroxyl. For example, using an interfacial polymerization process, encapsulated (DAHP) by polyurethane urea membrane. An elevated synthesis yield (22 percent) of a microcapsule powder was produced with a fill content of 62 wt percent of DAHP as calculated by elementary examination. DAHP microcapsules average size is 13.35 mm. In addition, By using lower temperatures and large scale-up capacity, spray cooling microencapsulation is considered the best encapsulation engineering. Nonetheless, microparticles can pose some drawbacks during processing, including low capacity for encapsulation and expulsion of the center. Spray cooling was used mostly to encapsulate minerals and vitamins. Spray cooling microencapsulated tocopherols with encapsulation quality levels greater than 90% in a lipid matrix. Microcapsules have been formed through spray cooling containing magnesium, iodine and retinol to stabilize by using salt of hydrogenated palm oil. Collected microcapsules are more stable and there

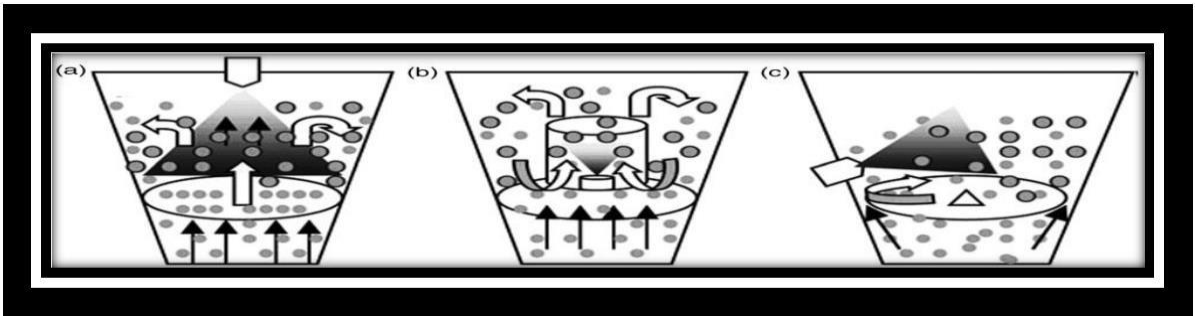
were no sensory variations observed. It has been shown that the encapsulating agent malto dextrin is effective in preventing linseed oil oxidation through spray cooling. (Sabee, M. M.,et.al;2016)

c) Fluidized bed technology

The water covering is drawn over the particles and fast dissipation will in general make an external surface. The coating thickness and formulations can be collected as needed. Top spray, foundation spray and tangential spray are various types of liquid mattress coaters.The cover surface is pulled down into the liquid bed in the top spray process, so that hard or porous particles are inserted into the sheet area. Improved enclosure performance and cluster development protection are accomplished through the inconsistent streams of surface materials and particles. The covered particles are dribbled based on the covering material's arrangement. The fluid-bed coaters with a spray nozzle at top yield greater particle scores than either the lower or the tangential sprays.In honor of its design by Wurster(1953), the lower spray was also named' Wurster's Coater.' In this process, a nozzle with cylindrical shape and a plate with a base i.e perforated is used in the coater tank

Evaporation by solvents. Three phases are found in the solvent evaporation process. They are the heart, the coat product, the LMV. Price product must initially be dissolved in a non-soluble volatile solvent in the LMV process. A primary component to be encapsulated in the coating polymer solution to be dissolved or dispersed. This is applied to the fluid production phase of the automobile with chaos, and the solution is cooled to evaporate the silicone solvent. The fur fabric shrinks surround the heart and protects the core. 5-fluorouracil microspheres are made, utilizing three levels of ethyl cellulose as wall materials and using an atmospheric solvent evaporation technique. Stirring speed, stirring duration, product loads and polymer levels were tested for impact on drug release in two different type of media. Alcoholic solution5-fluorouracil and polymer were deposited onto liqid paraffin comprising 33.3 percent n-heptane. The molecules filled with the medication were triangular in nature and had a size of from 25 to 200 mm. Acidic media has shown a greater rate of release than neutral ones in opioid release analysis of aqueous media. The medication release analysis from a silicone membrane aqueous gel base pH 7.0 formulation has been occur to be successful for a gel microsphere material for the skin lesions treatments.

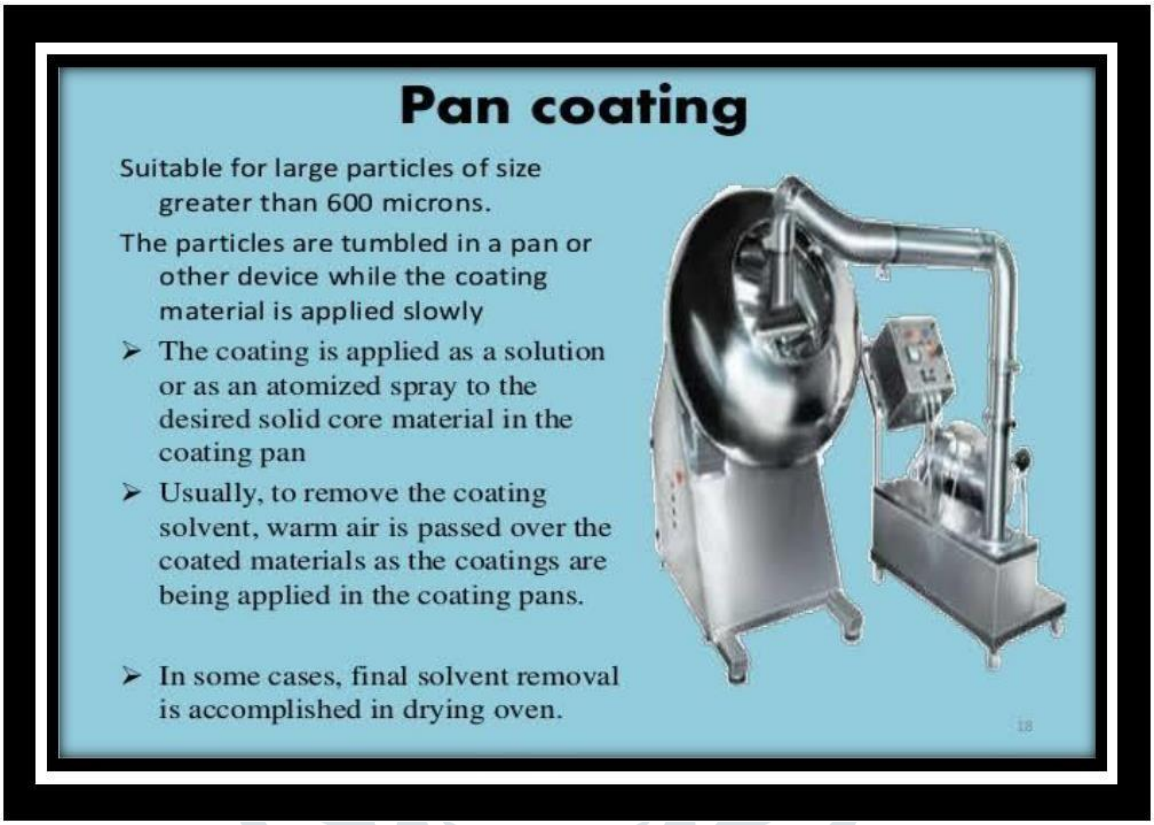
(a) Top spray **(b) bottom spray** **(c) tangential spray**



For examples A w/o/w emulsification process of solvent evaporation was used to interpose pseudoephedrine HCl, a strongly water-soluble substance, in poly (methyl methacrylate) microspheres.

Pan-coating

The solution of coating shall be used for painting panels as a spray for the hard core material. Warm air is pumped through the covered material to absorb the resin coating. This method can easily paint bigger particles.



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Details of certain other methods of encapsulation are

1) Extrusion

This is focused on a multivalented ion-related polysaccharide gel that immobilizes the center. Extrusion requires inserting the kernel into a sodium alginate solution and, through a decreased caliber pipette or syringe, a combination is forced to fall extrusion into a hardening liquid, such as calcium chloride. The relatively large particles of extrusion (usually 500 to 1,000 mm) are one of the drawbacks of this technique, which hinder use where mouth-feeling is important. Therefore, for the extrusion encapsulation, there is a very limited number of wall products. L. Microscopic. Calcium alginate gel acidophilus and extrusion-resistant starch aid in an increased rate of L survival. Upon 6 months of processing acidophilus in Iranian white savory milk. It has been shown that the β-cyclodextrin microencapsulation by extrusion gave an active oxidation remedy.

2) Lyophilization

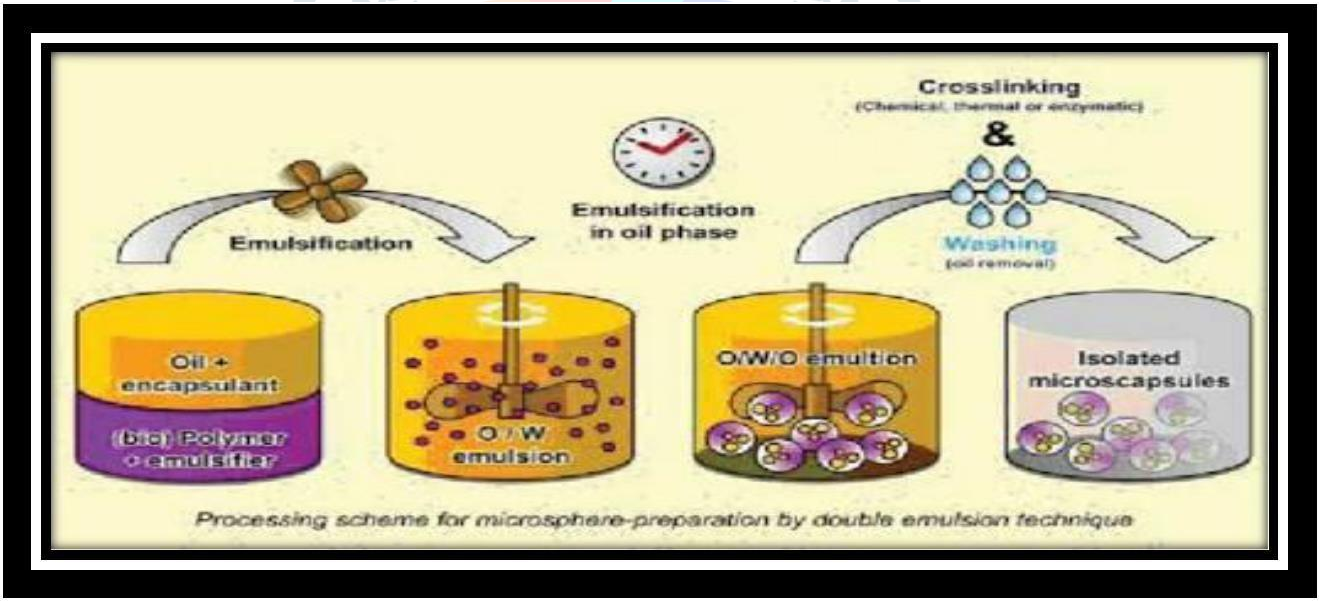
Frozen compounds are dehydrated under the sublimation vacuum cycle, that is, the extraction of

compound water without the application of high temperatures to test is dehydrated.This process provides good quality products, since it decreases high temperature fluctuations and is commonly used in essences or aromas. The high costs and tedious though, hinder the market applicability. In presence of malto dextrin, carboxymethylcellulose and lyophilizing, extra virgin olive oil is microcapsulated, which indicates that the oil has been unshaked for 9-11 months, improving shelf life. Encapsulated, with lyophilization, garcinia extract in whey protein isolation and malto dextrin, which has a higher volume, finer crumb consistency, attractive color and sensory qualities in rice.

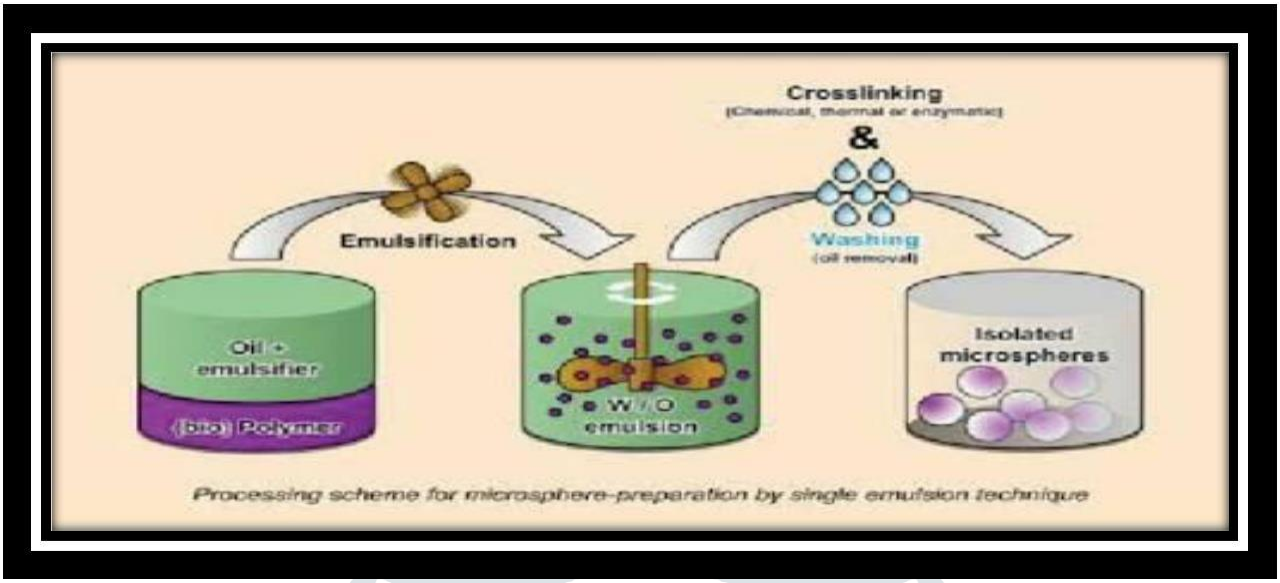
3) Emulsification

The center is first spread in an organic solvent in which the membrane is embedded through emulsification microcapsulation. Instead, the dispersion of liquid or oil with an emulsion stabilizer is emulsified. The organic solvent will be extracted through shaking evaporation to produce small polymer globules which encapsulate the center. Mainly enzysms, nutrients, vitamins and microorganisms are encapsulated by emulsifying. Through emulsifying the encapsulated enzymes, proteolysis was improved in contrast to the free output of the enzymes. Microencapsulated probiotics, showed further tolerance in artificial gastrointestinal conditions through emulsification in alginate chitosan. (Heidebach, T.,et.al;2009)

 # Single emulsion technique



 # Double emulsion technique



EFFECTIVENESS OF ENCAPSULATION INFLUENCE FACTORS

Similar criteria shall impact the encapsulation performance of the microparticle or the microcapsule or microsphere.

Factors that affect the quality of encapsulation are:-

1) Polymer solubility in organic solvent

The impact of solubility of the different PLGAs in methylene chloride was studied in accordance with calculation of a clouble methanol (Cs): higher Cs are expected to have a greater volume of methanol top recipients of the polymer solution. A relative elevated L / G ratio of PLGA poly- sea (75/25) demonstrated greater methylene chloride solubility than the other PLGA (L / Gratio 1⁄450/50). The Molecular weight polymer had a more prominent solvency than a sub-atomic weight polymer in methylene chloride. Methylene chloride was more soluble in end capped polymers, higher than the unend-capped polymers of the same weight and element reference. Dispersion of meds into the ceaseless procedure happened for the most part in the initial 10 minutes of emulsification, hence the encapsulation performance was relatively low as the polymer phase remained in an unsolid (semi-solid) state. Study shows that methylene chloride polymers with relatively high solubility took longer time to strengthen and less encapsulation, and the other way around. The size of particles and mass often varied depending on the polymer. Because substances with high solubility in methylene chloride remain longer in a half-solid state, the dyspheric stage was large oriented, which resulted in denser microparticles, before it was fully solidified.

2) Solubility of organic liquid solvents

The methylene chloride showed that, while methylene chloride was a stronger solvent for poly(lacticacid) as compare to other solvents, its encapsulation capacity was higher than chloroform or benzene. The fluid is more dissolvable than chloroform or benzene in methylene chloride. The' strong' solubility permitted a relative rapid mass transfer between the scattered and the constant stages,

contributing to fast polymer precipitation. The significance of dissolvability of the natural dissolvable in water was likewise affirmed by the expansion of water miscible co-solventslike CH3)2CO, methanol, ethyl acetic acid derivation or dimethyl sulfoxide (DMSO).In the awareness that methanol is an unsolvent for PLA and is a liquid miscible solvent, a dual role of the methanol to allow polymer precipitation can be expected to be: First, in the scattered process the presence of methanol decreased polymer solubility. Second, methanol facilitated water dissemination into the dispersed phase as a water miscible solvent.

3) Polymer concentrations

The efficiency of encapsulation increases with increasing concentration of polymers. Incapsulation capacity, for instance, improved from 53,1% to 70,9% when the polymer concentration increased from 20,0% to 32,5%. Low viscosity and quick solidification of the scattered state have decreased micro-particle porosity. There are two different ways to translate the commitment of a high polymer fixation to the epitome limit. The solvent precipitates on the scattered liquid layer quicker when strongly condensed and inhibits compound diffusion over the phase boundary.

4) The dispersed-phase ratio (DP-CP ratio)

The encapsulation efficiency, for example, was more than twice increased as the ratio from DP to 1/300 decreased from 1/50 to 1/300. A large volume of continuous phases is probably produced by diluting the solvent and supplying a high fixation slope of the natural dissolvable over the stage limit. The literature presents a related conclusion. The creation of microparticles in this case, which used ethyl acetate as a solvent, depended on the size. Nevertheless, microwaves easily hardened and developed erratic precipitates when the continuous process reached 80 ml or more. This is due to the large volume of the continuous process supplied the ethyl acetate with almost a sinkal state and immediately removed the solvent. The particle size has decreased as the density of the continuous process decreases with the rapid solidification of the polymer. Lwer bulk density (0,561g / ccat1/50vs0,357g / cc) of microparticles derived from a low DP / CP ratio.

5) Solvent extraction speed

The solvent removal process and level impact the solidification rate and the morphology of the micromicroparticles resulting from the dispersed stage. The solution can be extracted by the emulsion solvent evaporation / extraction process. (i)evaporation during the evaporation of the solution around its boiling point, or (ii) continuous phase removal. A temperature ramp or evaporation level in the former and the density of the dilution medium in the latter will regulate the extraction speed of solvents. Emulsification accompanied by various processes for extracting solvents was conducted to build PLGA microparticles containing salmon calcitonin .The solvent has been expelled by raising the heat from 15 to 40 kg at different rates during temperature-dependent solvent removal. The resultant microparticles had a hollow heart and a flexible surface. Depending on temperature ramp the core size and wall thickness was determined. A massive increase in temperature contributed to a thin wall and a big gap core, which culminated in a diminishing core volume with steadily rising temperatures (15-25,

then 40 BC). The hollow heart is thought to have been stuck inside solidified microparticles because of the quick expansion of methylene chloride. The weakening of the consistent procedure, that remains all the smallparticles in the sensitive state for a critical stretch of time, relentlessly and logically separated solvents through managed evacuation of the dissolvable. The resulting microparticles display a very poreful wafer like a porous inner structure. In the later study, porosity was observed as depending on the quantity of water spread from continuous phases to the dispersed phase that could only be completely solidified before the dispersed phase. It indicates that the gradual solidification of the microparticles is attributed to their strong porosity. While quick polymer solidification is generally assumed to result in high encapsulation performance, the study is not concerned with this. For this situation the dissolvable dissipation temperature didn't influence the exemplification execution. For this situation the dissolvable dissipation temperature didn't influence the exemplification execution. This can impact the paces of polymer hardening as well as of protein diffusiveness and its water solubility because of the diverse preparing temperatures. While the high temperatures rendered the dispersed state speedier to harden, the dissemination of the protein in the persistent procedure diminished and the beneficial outcome of the quick cementing was undermined.

6.**Drug polymer interaction**

Protein-polymer interaction leads to the improved efficacy of encapsulation. Proteins are in fact capable of interacting with ionic substances and encapsulated stronger inside polymers comprising free end groups of carboxylic than the end polymers. Then again, if the hydrophobic collaboration is the predominant power between the protein and the polymer, the increasing efficiency of encapsulation would gain fairly hydrophobic finishing polymers. In terms of the strong solubility of sCT in the continuous process, for instance, more than 60 per cent encapsulation efficiencies for salmon calcitonin (sCTs) have been reached. The close relation of sCT with hydrophobic polymers such as PLGA is due to that. On the other side, these protein- polymer interactions that restrict the release of protein from the microparticles. In some cases, the interaction between protein and polymer can be mediated by a co-encapsulated excipient. The potency of the encapsulation was improved by the co-encapsulation of tetanus toxoid in PLGA microparticles of gamma-hydroxy propylcyclodextrin (g-HPCD).

Drug degradation happens during the intermediate, semi-solid stage of dispersion. When, in the continuous stage, the solubility of the drug is greater than in the dispersed process, medicine can easily spread into this continuous phase. For example, in the continuous alkaline state (pH12, the encapsulation capacity of quinidine sulphate was 40 times more than in the neutral stage (pH7, in which quinidine sulphate is highly soluble).

7.)Molecular weight of polymer

PLGA Microsphere Injectable for longer Alzheimer's Disease Treatment contemplated the molecular weight effect of the polymer on exemplification productivity and built up a microsphere of o/w emulsion dissolvable evacuation process for interminable treatment. SEM has been utilized to

observed the surface structure of the microspheres. A co focal laser scan microscope was used to track the delivery of the medication within microsphere. The results showed the flat, circular presence of the PLGA 15 000 microsphere with a small particle size of about 50 mm. In the PLGA 15,000, 20,000, and 30,000, the encapsulation rate was 62,75, 27,52 and 16,63% respectively. The inhomogeneous distribution of the pharmaceuticals in microspheres was explained by the initial burst of the pharmaceutical microsphere. As the polymer fixation expanded in oil and PVA focus diminished at watery level, the embodiment execution of the microsphères improved. Through increasing the polymer density, burst release could be regulated. The product release profiles had a major effect on evaporation rate. Further testing under 30 kilometers. The efficacy of encapsulation decreased and product release improved with the decrease in the particle size within a certain number of particle sizes. In many industries, in particular the food- and pharmaceutical industry, microcapsulation technology is popular, as this enhances solubility, stability and controlled release properties of compounds including essential oils, antioxidants, antibiotics and medications. Application Microencapsulation technology is commonly used in several industries. The application of microencapsulation in these industries is therefore based in this paragraph. (Heidebach, T.,et.al;2009)

APPLICATIONS OF MICROENCAPSULATION ARE

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Uses in the food industry

Active additives are used in the food industry to improve the taste, color, appearance and shelf- life of items. In contrast, foods of great interest with practical health benefits, for instance antioxidants and probiotics. Most of these materials however have poor durability and environmental factors are readily decomposed. Therefore, it is essential to prepare bioactive high-stability compounds. One way of tackling these issues is through microencapsulation. There have been extensive research in recent years in the manufacture and applications in the food industry for high-efficiency microcapsules.

1. **Beverages**

The stability of anthocyanin was assessed, which was encapsulated in an isotonic soft drinking system within different carrier agents. The pigments derived from plants are water-soluble. For foods and drinks the colorants of these pigments are typically used because they have low toxicity and high water solubility for high color strength. In addition, several studies show that

antioxidants and anticarcinogenic properties of anthocyanins are significant. Nevertheless, anthocyanins form reactive pigments and can, by many influences including pH, temperature, air, oxygen and the food matrix, be decomposed into incolourable compounds. Consequently, the stability of such substances was improved using microencapsulation. The technique of spray- drying was used to encapsulate Cabernet Sauvignon anthocyanins. The microcapsules collected displayed standardized particle sizes and spherical layer. In addition, an improved defense against anthocyanin pigment was found through a mixture of Maltodextrin (MD) and Gum Arabic (GA).

Prepared curcumin and catechin microcapsules using (W/O/W) emulsions. The goal of this research was to avoid both curcumin and catechin degradation in drinking systems. When used in tandem, the biological activities of curcumin and catechin improve. Such two compounds are used in the food industry as powerful bioactive compounds, which can resist multiple diseased diseases like cancer, obesity and inflammation and cardiovascular diseases, to produce food and drink products. Curcumin and catechin are nonetheless toxic. The presence of oxygen, alkaline pH and high temperatures they are quickly destroyed. In this study it has been found that, individually or in combination, the stability of the encapsulated curcumin and catechin increases in a model drink system.

Spray-drying procedure encapsulated maltodextrin lemon oil. The clean and strong scent of lemon oil. It is therefore used primarily in food and beverages as a flavoring agent. Nevertheless, oxidation during stocking is caused by high levels of insaturated and oxygen working compounds in this fuel. This question has thus been solved by the microencapsulation technique. The specimen consistency in formulations of instant ice Tea premix at different storage temperatures (4, 28 or 45 ° C) has been tested in terms of sensory characteristics. It has been observed that embedded lemon oil has an acid odor / good profile and does not alter appearance during all storage conditions. These findings have shown that encapsulated lemon oil is available for 6 months.

2. Baked goods

Produced by spray-drying, using modified starch as an encapsulative agent, microcapsules of lycopene. Through adding the microcapsules to cake, the usability was calculated. Various fruit and vegetables produce lycopene as a carotenoid. It is usually used as a coloring red fruit. Nonetheless, because its high number of conjugated double bonds, lycopene is readily decomposed by oxidation during the processing cycle. The research predicted the stability of lycopene to be improved by microencapsulation. The results indicate a more pigmented cake developed with microcapsules than regular cake. Encase vegetable shortening in the manufacture of short dough biscuits to improve the oxidative strength and transform fat into steady flour. Many products are actually in dry form for the manufacture of commercial biscuits. The fluid (oil) or block (fat) must be applied to the fat components, though, which involves a further manual phase. This research aimed to create highly fat powder sand microcapsules that evaluated their impact on the performance of the biscuit compared to the quality of a hydrogenated vegetable fat test biscuit. Microencapsulated fat developed at low homogenizing pressure, containing 5 percent protein (WPC) as encapsulating agent, could be used to manufacture biscuits with appropriate characteristics. As the replacement for fat / oil for industrial biscuit development, microencapsulated high-fat powders could therefore be used.

3. Meat and poultry

Increasing nutritional value using probiotics in dry fermented sausages Nevertheless, several studies have found that the viability of probiotic species in fermented foods is low. The strategy of microencapsulation has been used to maintain the bacterial cells within a defensive membrane or matrix in order to improve the viability of these cells. The results indicate that Lactobacillus reuteri microencapsulated can be utilized in dry fermented foods because it can prevent loss of cell viability after drying, without affecting product sensory quality. The omega-3 fatty acids in fish oil microcapsules for enriching chicken nuggets and the impact on the oxidative stability and sensory properties of this material of frozen processing time compared with the added bulk fish oil. During the processing process, the sensory value of chicken nuggets enriched with omega-3 fatty acids was not compromised. Omega-3 fatty acids could be microencapsulated from fish oil to enrich pre-fried frozen meat with fish oil and to enhance oxidative shelf-life and to maintain the sensory properties of the enriched goods. The structural and sensory strength of chicken furters was assessed for the impact of the encapsulated ascorbic acid. Ascorbic acid is a healthy fruit and vegetable antioxidant. It's very unpredictable, though. Different factors, including temperature, light, high oxygen content and high water movement, decompose quickly. For frankfurters, ascorbic acid is often used as a replacement for sodium erythorbate. Therefore, this experiment was intended to encapsulate ascorbic acid in Frankfurt, as this technique facilitates the integration of a vitamin-functionally active antioxidant and increases consumer stability. The findings have shown that ascorbic acid can be used as an antioxidant to generate frankfurters with appropriate sensory characteristics.

4. Dairy products

Flavourzyme microcapsules produced for use in cheese production with different wall materials. For the production of the necessary color, texture, taste and aroma, low-moisture cheese species such as cheddar need longer ripening. Because conventional cheese ripening takes place at a very slow rate, the maturation rate is increasing by the introduction of exogenous enzymes. The direct introduction of enzymes, however, leads to loss of enzyme, poor distribution of enzymes, reduced development, and poor quality of cheese. During the manufacture of cheese, microcapsules applied to the milk permitted good flavourzyme distribution.

The results of spray-drying microcapsulation on probiotic bacteria's stability in icecream was analyzed. Many ice creams have been developed lately through the introduction of probiotic bacteria. The effectiveness of the probiotic bacteria is impaired however by processing and storage. Therefore, microencapsulation has been utilized to upgrade the endurance of probiotic microscopic organisms. The results showed that the encapsulated probiotic bacteria had higher survival rates compared to the non-encapsulated culture.

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✓ **Application in pharmaceutical industries**

- The technique of micro-encapsulation in the pharmaceutical industry is widely used to control the release of drugs, improve stability and mask the taste. The use for the colon- specific distribution of a water solution peptide product was explored using microcapsules formulations. Peptides are typically heat-sensitive and low-permeability by polymer membranes. This research therefore aimed at maintaining the safety of heat- sensitive drugs and the optimal permeability, allowing macromolecular medicines to be postponed. The results indicate the good film formability in the 95:85:40 molar ratios of the poly(EA / MMA / HEMA) at 40 ° C. The correct approach could be recommended to prepare delayed release of colon-specific microcapsules with water-soluble drugs.
- Microcapsules of chitosan co-loaded for synergistic cancer therapy are developed by doxorubicin and heparin. Scientists attempted, with microencapsulation to preserve healthy Tissues, to remove adverse effects of doxorubicin (DOX) toxic chemical- therapeutic agent. In contrast, heparin (HEP) is harmful and renders cellular absorption impossible. Therefore, a HEP / CHI multilayered capsule was used for shaping chitosan (CHI), a polymer that was charged positively. CHI will defend HEP from heparanase, which makes it easier to transmit HEP intracellularly. In combination therapy the anticancer drug DOX is also encapsulated. In this analysis the investigators found that the heparanase solution was highly stable throughout microcapsules filled with DOX (HEP / CHI). Therefore, the synergistic influence on human pulmonary carcinoma (A549) cells was observed in the microcapsuls of DOX and HEP.
- Detection of bitter taste masking of active ingredients prescription ingredients ibuprofen and roxithromycin, the traditional anti-inflammatory, non-steroidal, infectious drugs and popular anti-inflammatory medicines. It was observed that the chemical photos obtained by measuring pure API solutions are significantly different from those obtained by measuring APIs encapsulated with taste-masking additives. In contrast, in both APIs, the shift character received from microencapsulation was the same.

✓ **Some applications commonly used are**

1) Export paper without carbon
2) Scratching and sniffing
3) Flavors and perfume
4) Of medical uses, microencapsulation
5) Microencapsulation: daily use (capsulation of vitamins, encapsulation of minerals (iron)
6) Microencapsulation was also used to reduce potential risks involved with the treatment of hazardous or noxious materials. Thanks to the treatment of fumigants, herbicides, insecticides and poisons, toxicity has been reduced advantageously after microencapsulation
7) Formulation (pharmaceutical preparations for oral and injection)

8) Drug flavor masking (taste tinidazole masking and microencapsulation process optimization)
9) Protection
10) Comfort
11) Reactant exclusion
12) Enhanced microcapsule surface usability
13) For lower toxicity
14) To reduce volatility
15) Reducing uncertainty.
16) Reducing flammability. Prolonged dose ways of release. It is necessary to prescribe the microencapsulated medication because microencapsulation is perhaps most effective in the preparation of pills, capsules or types of parenteral administration.
17) Seventeen. Separating volatile materials in order to remove incompatibilities
18) Converting liquid to solid
19) Providing environmental protection of atmospheric-sensitive product stabilization
20) To reduce irritation of the gastric and other GI tract
21) Targeting drugs
22) Meat, consumer products, and cosmetics industry encapsulation
23) Encapsulation systems of agricultural products
24) Microencapsulation approach for the preparation of an intrauterine contraception system was also suggested.
25) Many applications are essential to improve space capacity.

- To improve the stability of emulsions.
- To improve flowability.
- To adjust the level of chemical reactants solubilization
- Eliminate unpleasant taste or odor while taking a drug.
- To extend the impact of a drug (the capsule is not completely opened, so the contents can slowly leach out.)
- To preserve the medication from environmental degradation.

ADVANTAGES

1. Safety of brittle, sensitive materials from their conditions during usage
2. Process efficiency enhanced by improving solubility, flow capacity etc

3. Shelf life of the drug enhanced by avoiding reactions like oxidation, dehydration
4. Masks the odor and bitter taste of drug
5. Immobilization of Enzyme or microorganism
6. The outer layer of microcapsule can be changed by addition of some ligands such as antibodies to target specific for some organs and other body parts
7. Handling of liquids drugs as solids by microencapsulate it

DISADVANTAGES

Most of the disadvantages of microencapsulation are a result of the manufacturing methods which are as follows:

1. Generally, many methods utilize solvents of oganic nature which may not suitable for drug or confirmly denature proteins and also too harmful in vivo i.e inside body if any residual solvent from the process remains as such in the microencapsules.
2. Microcapsules sterilization: by gamma irradiation can trigger deterioration of the polymer/ coating material and microcapsule product.

NEW TECHNOLOGY / RECENT DEVELOPMENTS

Many technologies are being established lately and some are being regarded. These are the following

1. Novel process of protein microencapsulation utilizing electrostatic field with high voltage.
2. Aminoglycosides encapsulated by liposome
3. In vitro

(a) Hydrophilic core material like

(i) Doxorubicin

(ii) Cisplatin

(iii) 5-Fluorouracil

(b) Hydrophobic core material

(i) Taxol

(ii) Comptothecin (CPT)

(iii) In vivo release

4. Dispersal Technology
5. Solution Gel Microparticulate Development New Methods
6. Biodegradable Microcapsules Formulation

(i) Calcium Alginate Microencapsules

(ii) Chitosan microencapsules

(iii) Albumin microencapsules

7. Technique for evaporation of solvent emulsion utilizing surface reaction study
8. New approach based on a mixture of poloxamer I Plga as a toxoid delivery vehicle for tetanus
9. Design of a continuous oral release system

(i) Matrix preparation by direct compression

(ii) Matrix preparation by liquid granulation

FUTURE TRENDS

- **Food industries:** A long-term phenomenon with significant market opportunities continues to be the growth of functional foods. Therefore, in the food industry, new innovations have been introduced; microencapsulation is one of the developments of interest at the moment. In addition, several scientists continue to develop innovative components for use in food products utilizing microencapsulation techniques as active additives, preservatives, colorants, and flavors.

Food Industry	Pharmaceutical Industry	Other Industries
Functional foods	Specific drugdelivery	Textile industries
Probiotics	Oral drugdelivery	Fragrancefinishing
Antioxidants	Transdermal drugdelivery	Color change materials
Vitamins	Stomach-specific drugdelivery	Fireretardants
Dietaryfibers	Colon-specific drug delivery	
-Food preservatives	S intesti spec m ne ific all	Cosmetic industries
-Food colorants	drugdelivery	Essential oils

- **Pharmaceutical industries** Microencapsulation of medicines has potential for apply in the pharmaceutical industries as it helps for the consistent and regulated delivery of medications in various medical conditions. For organ-specific drug distribution, however, encapsulated medicines still have drawbacks. It remains a problem to achieve high reproducibility for microencapsulated medicines.For contrast, in other sectors, including the apparel and pharmaceutical industry, microencapsulation is used.

CONCLUSION:-

Microencapsulation technique helps in overcoming the causes which are caused by conventional dosage form such as poor bioavailability, low solubility, poor flow property, uncontrolled release of drug. Yes, it is true that all drugs cannot be encapsulated in microencapsule but the drugs which are prepared by this technique proves to be good in terms of their properties as compare to conventional dosage form. E.g. Isosorbide dinitrate microencapsule has sustained release action.

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