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NANOCAPSULES AS NOVEL DRUG DELIVERY SYSTEM

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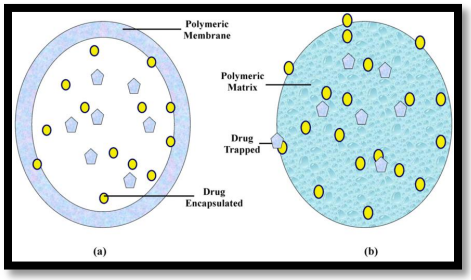
ABSTRACT

Nanocapsules are vesicular system in which the drug is confirmed to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. Nanocapsule consist of a thin membrane surrounding a core (liqid, solid) with their size ranging from 10nm to 1000nm .Two technologies can be used to obtain such Nanocapsules: the intefecial polymerization of a monomer or the interfacial nano deposition of a performed polymer. Nanocapsules can be prepared by four different principally different approaches: interfacial polymerization, interfacial precipitation, interfacial deposition, self assembly procedure. All these procedure offer their individual advantages and disadvantages when it comes to the design of optimized drug carrier system. The most important capsule parameters such as capsule radius disrtribut-ion, the capsule surface, the thickness and the permeability of the capsule membrane and its thermal or chemical decomposition, are discussed and example are shown.

INTRODUCTION:

A Nanocapsule is a nanoparticle that is spherical, hollow structure with a diameter less than 200nm in which a desired substance may be placed.They can filled with a solvent, either polar or non polar (fig.1). Nanocapsule can be distinguished from other nanoparticle because they have well defined core and shell, whereas the latter do not. Nanocapsule has been developed as drug delivery systems for several drugs by different routes of administraton such as oral and parental. Reduce the toxicity of drugs. Polymeric nanoparticles are named nanocapsule when they contain polymeric wall composed of non-ionic surfactants, macromolecules, phospholipid and an oil core.

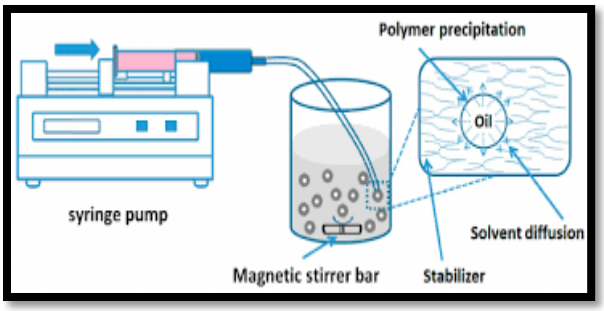


(fig.1)

PREPARATION OF NANOCAPSULE:

1.Nanoprecipitation method:

Nanoprecipitation is also called solvent displacement or interfacial deposition method, whichwas first developed and introduced by Fessi's group. The principle of fabrication method is known as Marangoni effect.In the nanoprecipitation method, the nanoparticles are obtained in the colloidal suspension when the oil phase is slowly added to aqueous phase under moderate stirring(fig.2). Formation of the NPs is instantaneous and needs only one step so it has the advantage of the rapid and easy operation. The key parameters in the fabrication procedure have great influence on the nanoprecipitation method, such as organic phase injection rate, aqeous phase agitation rate and the oil phase/aqueos phase ration. particle sizes of very narrow distribution can be synthesized because of the absence of shearing stress. This method is used mostly for hydrophobic drug entrapment, but it is also employed sometimes to incorporate hydrophilic drugs. Through rapid solvent diffusion, the NPs ase formed immediately. After that, the solvent are removed under reduced pressure.

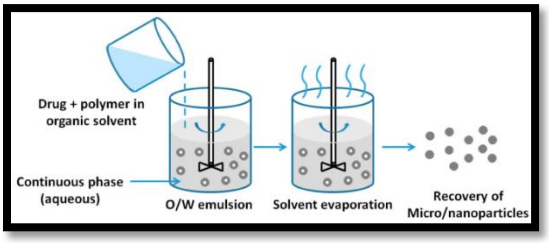


(Fig.2). Preparation of NPs by nanoprecipitation method

2.Emulsion diffusion method:

Emulsion evaporation has been used for a long time to form polymeric NPs from as-prepared polymers.

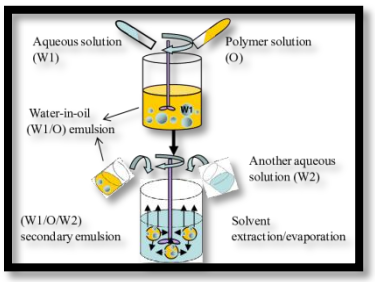
The method is based on the emulsification of polymer organic solution into a water phase, followed by organic solvent evaporation. The polymer is first dissolved in a suitable solvent (e.g., ethyl acetate, chloroform, or methylene chloride). The organic phase is poured into the continuousphase (aqueous phase) in which a surfactant is dissolved to impart stability to the emulsion. Emulsification is carried out under high-shear force to reduce the size of the emulsion droplet. This process will largely determine the final particle size. After the formation of emulsification, the system evaporates the organic solvent under vacuum, which leads to polymer precipitation and nanoparticle formation. The schematic of the emulsion evaporation processes is illustrated in Figure 3.



(fig.3)

3.Double emulsification method:

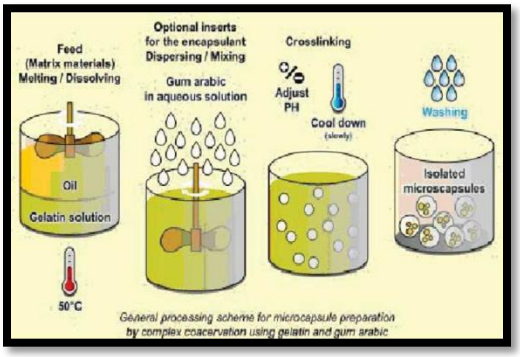
Double emulsion are complex heterodisperse system called "emulsions of emulsions", that can be classified into two measure major types: water-oil-water emulsion (w/o/w) and oil–water-oil emulsion (o/w/o) .Thus the dispersed phase is itself an emulsion and the inner dispersed globule /droplet is separated from the outer liquid phase by a layer of another phase. Double emulsions are usually prepared in a two step emulsification process using two surfactants: a hydrophobic one designed to stabilize the interface of the w/o internal emulsion and a hydrophilic one to stabilize the external interface of the oil globules for w/o/w emulsions.Their is schematic representation in fig.4



(fig.4)

4.Emulsion-cocervation method:

The emulsion-cocervation process is mainly presented as a strategy for nanocapsule preparation from naturally occurring polymeric materials. Up to now, sodium alginate and gelatin have been used through synthetic polymeric materials could be used for this purpose. The procedure involves the o/w emulsification of an organic phase with an aqueous phase by mechanical stirring or ultrasound. It it represented in (fig.5)



(fig.5)

The table below displays how nanocapsules exhibit different traits based on the method by which they were prepared. Nanocapsule types vary by size, drug concentration, and active substance release time.

	Mean size (nm)	Drug concentration in diluted dispersion (mg/ml)[5]	Drug concentration in concentrated dispersion (mg/ml)[5]	Active substance release time (90%) (min)[5]
Nanoprecipitation	250	0.002–0.09	0.15–6.5	750
Emulsion-diffusion	425	~0.2	50	60
Double emulsification	400	2–5	20–50	45
Emulsification coacervation	300	~0.24	12	>2000

APPLICATIONS OF NANOCAPSULE:

1.Nanocapsule as a drug delivery system:

Dispersed polymer Nanocapsule can serve as nano-sized drug carriers to achieve controlled release as well as efficient drug targeting. The dispersion stability and the primary physiological response are mainly determined by the type of the surfactant and the nature of the outer coating. Their release and degradation properties largely depend on the composition and the structure of the capsule walls. Nanocapsules can be prepared by four principally different approaches: interfacial

polymerization, interfacial precipitation, interfacial deposition, and self assembly procedures. The most important capsule parameters such as capsule radius distribution, the capsule surface, the thickness and the permeability of the capsule membrane and its thermal or chemical decomposition, are discussed.

2.Nanocapsule for delivery drug:

Scientists in Australia have developed minute Nanocapsules which can be used to target anti-cancer drugs to tumors, sparing other healthy tissue from side effects. The capsules, which measure about 1 micron across - or 1 thousandth of a millimeter - can be coated with an antibody which directs them from the bloodstream to a tumor. Once they are in the tumor, a quick blast with a harmless skin-penetrating laser producing near-infrared light causes the capsules to open up, discharging their contents. To make them, a polymer which when added to a suspension of drug particles forms a sphere enclosing the drug, several layers thick.

A)Cancer: Water-soluble polymer shells are being created to deliver a protein, apoptin, into cancer cells. The protein goes into the nucleus of the cancer cells while leaving healthy cells alone, unlike other conventional therapies as gene therapies and chemotherapy. The capsules are 100 nm in size. Active targeting of cancer cells is also being researched. Through active targeting, the nanocapsules form ligands that bind to malignant cells for cell delivery. This method is especially beneficial for those drugs that are not as permeable through the cell membrane, and where tissues are diseased, the nanoparticles are able to bond easier with the malignant cells.

B)Food usage: Nanoencapuslation in foods involves the changing of textures, flavorings, colorings, and stability in shelf-life

C) Neutraceuticals: Nutraceuticals are substances that are placed in food to enhance nutrition. The increased bioavailability of these substances is relative to the size of the nanocarrier. The smaller the nanocarrier, the better the delivery properties and the solubility of the nutraceuticals; the nanocarrier is able to enter the bloodstream easier if smaller.

D)Ethyl alcohol absorption: Relatively new research involves the encapsulation of digestive enzymes within a non-toxic polymer shell. The enzyme filled nanoshell has been proven in lab mice to absorb ethyl alcohol from the bloodstream, therefore resulting in reduced blood alcohol levels. It has been concluded that the particles act as organelles, which proposes other benefits to enzyme therapies. This discovery is introducing other studies, such as encapsulation methods for hair loss.

CHARCTERIZATION OF NANOCAPSULE:

1.Absorbability: aspect ration affects the ability of the nanocapsule to penetrate tumor cells. Low aspect ratios (spherical capsules) tend to penetrate cells more easily than high aspect ratios (rod-shaped capsules).

2.Structure: The nano-sized structure of nanocapsules allows permeating through basal membranes, which makes them effective carriers of medicine in biological systems. The specific processing of nanocapsules gives them unique properties in how they release drugs in certain situations. Generally, there are three physico-chemical release mechanisms that are used to release the drug or medicine from the polymeric shell of the nanocapsule.

3.Delivery**:**

a]Hydration and diffusion – In this the release mechanism the nanocapsule will swell due to the effects of hydration. Once the nanocapsule has swollen to a point where it stretches, the polymeric membrane will allow for diffusion of drug through the polymeric membrane and into the biological system.

b] Enzymatic reaction – The polymer shell must be first selected to coordinate with the enzymes produced by the human body to produce and

enzymatic reaction. This reaction will cause a rupture in the polymeric membrane which allows the drug to be dispersed into the system.

c] Dissociation of the drug – The drug dissociates from the swelled nanocapsule and diffuses out into the rest of the cell.

4.Determination of pH of nanocapsule:

Nano capsules formulation pH was measured using a digital pH meter at room temperature. Nano capsules dispersion Ph values fall within range of 3.0-7.5.

5.In-vitro drug release:

In vitro dissolution studies were carried out using USP type 11 dissolution apparatus. The study was carried out in 100ml of buffer (pH 3.0). The nano capsules suspension was placed in dialysis membrane and dipped in dissolution medium which was kept inert thermostatically at 37±0.5oC. The stirring rate was maintained at 100 rpm. At predetermined time intervals 5 ml of sample were withdrawn and assessed for drug release spectrophoto metrically. After each withdrawal 5ml of fresh dissolution medium was added to dissolution jar.

The use of nanocapsule as smart drug:

Nanocapsule can be used as smart drugs that have specific chemical receptors and only bind to specific cells. It is receptors that makes the drug 'smart', allowing it to target cancer or disease. The advantages of nano-encapsulation technologies for pharmaceutical applications include:

- Higher dose loading with smaller dose volumes
- Longer site-specific dose retention
- More rapid absorption of active drug substance
- Increased bioavailability of the drug
- Higher safety and efficacy
- Improved patient compliance

CONCLUSION:

Polymer nanocapsules asre promising carrier systems for applications in drug targeting and controlled released. Their preparation often relies on spherical phase as a template for the formation of a polymer. In drug delivery system, they are confined to suit the complexity of the applications as they intend to produce contents in response to a specific biomolecular triggering action mechanism. Nanocapsules also have the efficient applications in various fields of the agrochemicals, wastewater treatments , genetic engineering, cosmetics, cleaning product, as wall as in adhesive component. Nanocapsules can close the active substance in their interior and then release it in the desired time frame. These systems are used for the transport of biologically active substances. The ability to deliver active ingredients to the right place and their controlled release are very important features ensured by nanoparticle. They enable more efficient use of cosmetic active ingredients. The use of nanoparticles also permits deeper penetration of cosmetics into the skin. The possibility of closing the active substance in the shell made of natural, bioavailable, or biodegradable materials is a very attractive property of nanocarriers that permits more efficient use of the active compounds contained within the capsule. Another advantage of the use of nanoparticles is the protection they offer to sensitive material against the harmful effects of external factors or other ingredients of the cosmetic formulation. It is also possible to increase the stability of the cosmetics. The nanoparticles enable further control of odor and color materials. Active agents are mostly composed of an oil mixture and they have lipophilic character. In the carrier system, the location of the active agent consists of dissolution or immobilization in a matrix or adsorption on the surface of nanoparticles.

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