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Review Article

Nanocapsules Used in Drug Delivery System

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Nanocapsules 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. Another important criterion is the capsule size, where an optimum is generally seen for radii ranging between 100 and 500 nm. Nanocapsules can be prepared by four principally different approaches: interfacial polymerization, interfacial precipitation, interfacial deposition, and self assembly procedures. All these procedures offer their individual advantages and disadvantages when it comes to the design of optimized drug carrier systems. 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 and examples are shown. In combination with efficient preparation procedures, nanocapsule dispersions allow for new and promising approaches in many kinds of pharmaceutical therapies.

Key words: Nanocapsule, surfactant, interfacial polymerization, interfacial precipitation, interfacial deposition.

INTRODUCTION

Nanotechnology is the science and technology of precisely manipulating the structure of matter at the molecular level. [1] Nanotechnology is the study of extremely small structures. The prefix “nano” is a Greek word. The word “nano” means very small or miniature size. [2] Nanotechnologies are presented as providing unprecedented technological solutions to many environmental problems including climate change, pollution and clean drinking water. [3] Nanotechnology is the creation of materials, devices, and systems by controlling matter at the nanometer scale (1-100 billionths of a meter). [4] Nanotechnology is the science and technology of small things – in particular, things that are less than 100nm. in size. One nanometer is 10^{-9} meters or about 3 atoms long. [5] Nanotechnology holds promise in many areas like advanced diagnostics, targeted drug delivery and biosensors. [6]Nanotechnologies are the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanometer scale. [7] The

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term nanotechnology has come to have two primary meanings:

1) New science and technology that takes advantage of properties operating at the nanoscale,

2) Building with atomic precision through the use of molecular machine systems.(8) Nanotechnology is an engineering of functional systems at the molecular level, covers a broad range of topics and is focused on controlling and exploiting the structure of matter on a large scale below 100 nanometers.(9) The science, engineering, and technology related to the understanding and control of matter at the length scale of approximately 1to 100 nanometers.(10)Nanotechnology has incorporated advances in a variety of diverse scientific disciplines including molecular biology, chemistry, genomics, physics, material science, and medicine.(11)Nanotechnology – Building and using materials, devices and machines at the nanometer (atomic/molecular) scale, making use of unique properties that occur for structures at those small dimensions.(12)

NANOCAPSULE

Nanocapsules are colloidal-sized, vesicular system (heterogeneous) in which the drug is confined to a reservoir surrounded by the polymer. The core is a lipophilic liquid surrounded by a single layer of polymer. (13) First of all the nanocapsules can be likened to vesicular systems in which a drug is confined in a cavity consisting of an inner liquid core surrounded by a polymeric membrane. (14)

Advantages of Nanocapsules (15-17)

- Higher dose loading
- Reduce irritation of drug at site of administration
- Greater protection from degradation during storage
- Site specific action.
- Increase bioavailability of drug
- Control and sustain release of the drug at the site of localization.
- The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc

Disadvantages of Nanocapsules (18-20)

- Very costly formulation with no low yield
- Productivity is more difficult. As a industrial applications , technology transfer to commercial production is very difficult
- Reduced ability to adjust the dose
- Highly sophisticated technology
- Requires skills to manufacture
- Stability of dosage form is big issue owing to its nano size
- Recycling is very expensive

Methods for the Preparation of Nanocapsules

1. Nanoprecipitation method (21) (Fig. 1)

The nanoprecipitation method is also called solvent displacement or interfacial deposition.The polymers commonly used are biodegradable polyesters, especially poly-e-caprolactone (PCL), polylactide (PLA)and polylactide-co-glicolide PLGA.

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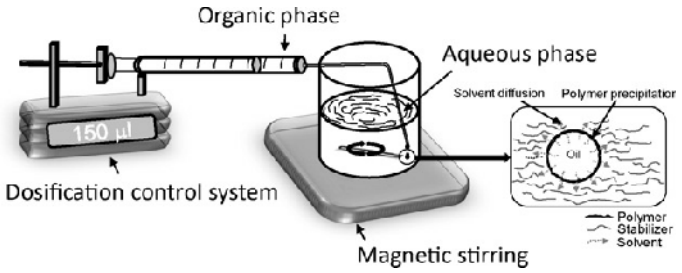

Fig. 1. Set-up used for preparation of nanocapsules by the nanoprecipitation method

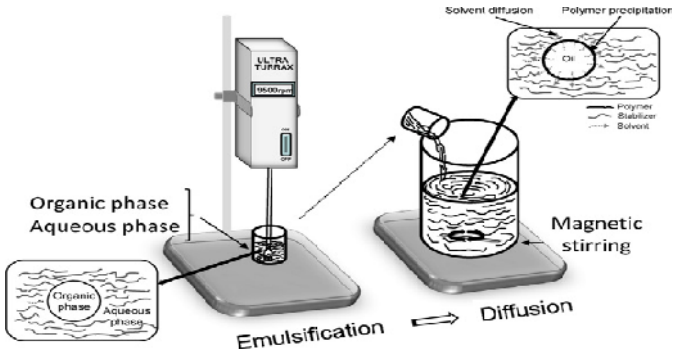

Fig. 2. Set-up used for preparation of nanocapsules by the emulsion–diffusion method.

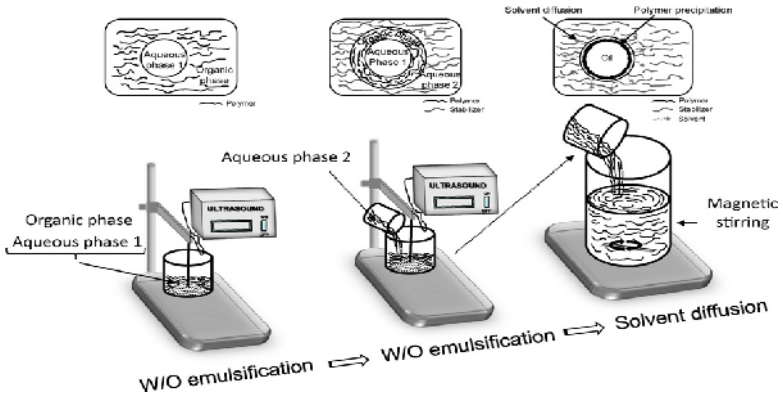

Fig. 3. Set-up used for preparation of nanocapsules by the double emulsification method.

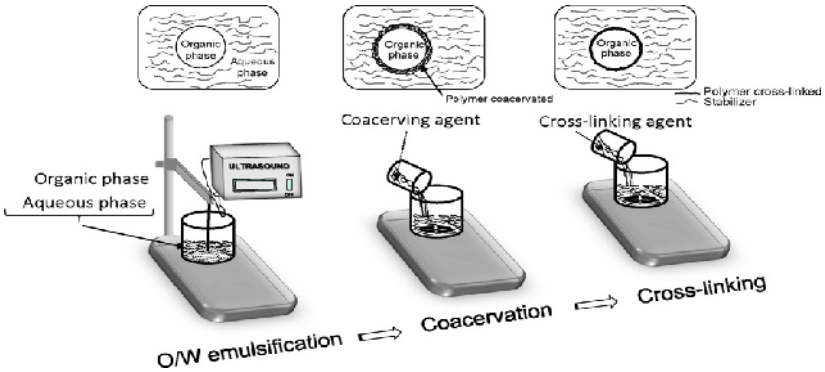

Fig. 4. Set-up used for preparation of nanocapsules by the emulsion-coacervation method

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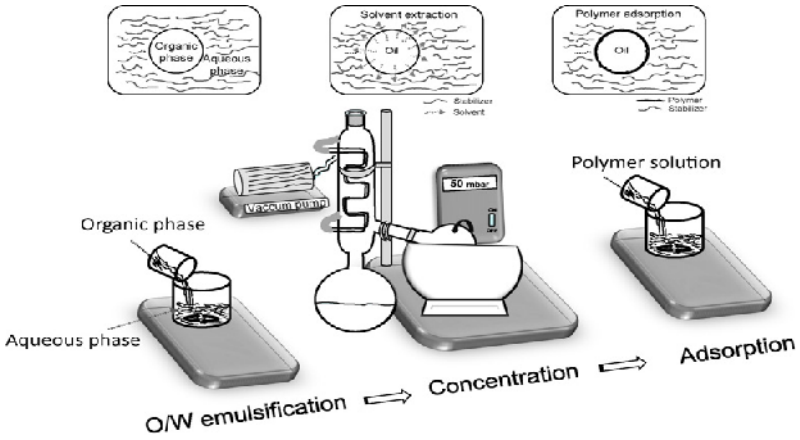

Fig. 5. Set-up used for preparation of nanocapsules by the polymer-coating method.

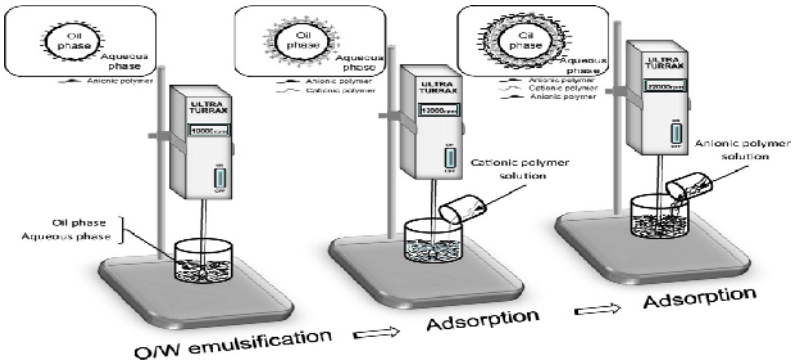

Fig.6. Set-up used for preparation of nanocapsules by the layer-by-layer method

2. Emulsion–diffusion method [22]

In this method, (Fig. 2) the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. Polymers commonly used are biodegradable polyesters, especially PCL, PLA and eudragit. Poly (hydroxybutyrate-co-hydroxyvalerate) (PHBHV) may also be used.

3. Double emulsification method [23]

Double emulsions are complex heterodisperse systems (Fig. 3) called "emulsions of emulsions", that can be classified into two major types: water-oil-water emulsion (w/o/w) and oil-water-oil emulsion (o/w/o).

4. Emulsion-coacervation method [24]

The method involves (Fig. 4) a mixture of two aqueous phases, of which one is the polymer chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO) and the other is a polyanion sodium tri polyphosphate. In this method, positively charged amino group of chitosan interacts with negative charged tri polyphosphate to form coacervates with a size in the range of nanometer.

5. Polymer-coating method [25]

The layer-formed polymers used by them are poly (methyl methacrylate) (PMMA), poly(methacrylate) (PMA) and PCL. Nanocapsule formation is based on the mechanism of engulfment in three-phase systems.

6. Layer-by-layer method [26]

The layer-by-layer method makes used of polycations such as polylysine, chitosan, gelatin B, poly (allylamine) (PAA) poly (ethyleneimine) (PEI), aminidextran and protamine sulfate. The following polyanions are used: poly (styrene sulfonate) (PSS), sodium alginate, poly (acrylic acid), dextran sulfate, carboxymethyl cellulose, hyaluronic acid, gelatin A, chondroitin and heparin.

Behaviour of Nanocapsules as Drug Delivery Systems

1. Mean nanocapsule size [27]

The particle size analysis of the formulations was performed using Malvern Mastersizer MS. The average particle size and size distribution of each nanocapsular dispersion was recorded.

2. Nanocapsule zeta-potential [28]

The volume particle size distribution of the spray dried powders was determined by photon correlation spectroscopy (PCS) using a Malvern Zetasizer Nano ZS. Prior to measurement samples were diluted 10 times with distilled water. Photon correlation spectroscopy (PCS) is based on the measurement of the Brownian motion of the particle.

3. Nanocapsule shell thickness [29]

Make theoretical approaches based on the hypothesis that the polymer is the unique component of the nanocapsules wall, estimate shell thickness by using TEM photomicrographs of nanocapsules. The over-estimation of shell thickness obtained by suggests that probably not all the polymer forms nanocapsules, meaning that nanosphere formation may also occur.

4. Nanocapsule dispersion PH [30]

The pH of the nanocapsule suspension was measured at 25^0 c using a DM-22 potentiometer.

5. Nanocapsule encapsulation efficiency [31]

The drug nanocapsules were separated from dispersion by ultracentrifugation at about 10000RPM for 1 hour in which nanocapsules settled at base in pellet form. While free drug remain in supernatant liquid. Entrapment efficiency was calculated according to following equation.

$$EE\% = \frac{\text{the amount of entrapped drug in Nanocapsules}}{\text{The total amount of drug included in preparation}} X100$$

6. Nanocapsule active substance release [32]

Free drug of the formulations was first determined in the supernatant by choosing a

solvent in which only the free drug gets dissolved and not the other ingredients. Ten millilitre of the supernatant was made up to 100 ml with 0.1 N HCl and filtered through Whatman filter (size 44); 1 ml of the filtrate was taken then made up to volume with 10 ml of 0.1 N HCl and analyzed for free drug present., In vitro release studies of the formulations were carried out at desired pH (phosphate buffers) at 37°C and the cumulative percent release of drug at different time intervals was determined.

7. Nanocapsule stability [33]

The use of exaggerated conditions of temperature, humidity, light, and others to test the stability of drug formulation is termed as accelerated stability testing. Accelerated temperature stability studies are generally conducted at 37, 50, and 60°C, as well as at room temperature and freezing temperatures. Short-term stability studies were carried out for the formulations for a period of 2 months. The nanocapsule formulations were stored at 4 and 25°C for a period of 60 days. At weekly intervals, 5 ml of sample was withdrawn and analyzed for the drug content. They were also observed for physical changes during the period of storage.

8. Nanocapsule performance evaluation [34]

Among the main challenges of administering nanocapsules as carriers of active molecules are the targeting of specific organs, allowing site-selective action of the compounds, minimizing their side effects, and providing sustained drug delivery in order to increase therapeutic availability, modification of tissue drug distribution, transmucosal delivery, and gastrointestinal mucosal protection and simply to obtain significant therapeutic activity.

Applications [35-38]

1. Cancer

Water-soluble polymer shells are being created to deliver a protein, apoptin,into cancer cells. The capsules are 100 nm in size.

2. Food usage

Nanoencapuslation in foods involves the changing of textures, flavorings, colorings, and stability in shelf-life.

3. Nutraceuticals

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.

4. Ethyl alcohol absoption

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.

5. Self healing materials

For materials such as components in microelec-

-tronics, polymeric coatings, and adhesives, nanocapsules can reduce damage caused by high loads. The healing of cracks within these materials is alleviated by dispersing nanocapsules within the polymer. The healing substances include dicyclopentadiene (DCPD), which is prepared on site within the material by sonication.

6. Nanocapsules have been proposed as drug delivery system for several drugs by different routes of administration such as oral, parenteral.

Conclusion

Nanoencapsulation is an attractive strategy for the vectorization of a variety of active substances. Although with different objectives, research has been focused on antineoplastics, antiinflammatories, immunosupresants, antigens, hormones, antivirals, antibacterials, antifungals, diuretics, antipneumocystics and vitamins, among others.

There is no ideal method because each one has its advantages and limitations. In general terms, for example, all the methods allow lipophilic active substance encapsulation, excluding the double emulsification method which had been developed for hydrophilic active substances such as proteins. In their majority, all procedures can be used with solvents with low toxic potential and without the addition of other chemical substances that allow an easy purification.

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