



# NANOCAPSULES: A PROMISING TOOL FOR DRUG DELIVERY

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## ABSTRACT

Nanocapsules are tiny colloidal systems designed to transport drugs, featuring an oily or aqueous core encased in a thin polymeric membrane. They are notable for their protective coating, which often prolongs the release of active ingredients while shielding the drug from harsh conditions. Several technological approaches are employed to create nanocapsules, with interfacial polymerization being the most widely used. The size distribution stands out as the key characteristic in their production, assessable through various techniques such as X-ray diffraction, scanning electron microscopy, transmission electron microscopy, among others. A nanocapsule that can be consistently reproduced is suitable for numerous biological applications. They find utility in a variety of areas, including botanical pesticides, genetic modification, cosmetics, cleaning agents, wastewater management, and adhesives, among others. This review serves as a comprehensive guide to nanocapsules, detailing their benefits, preparation methods, evaluation techniques, and characterization.

**Key words:** Advantages, Polymers, Composition, Methods of preparation and Evaluation

## INTRODUCTION

The word "nano" which means small, is the Greek word. "Nanotechnology" includes advancements in technology at the nanoscale, typically between 0.1 and 1000 nm. In the domains of biomedicine, pharmacology, electronics, and molecular diagnostics, nanomaterials have found numerous significant uses. The term nanoparticle is a combination name of both (i) nanospheres and (ii) nanocapsules.

(i). Nanospheres have a matrix type of structure in which drugs may be encapsulated within the particle or adsorbed at the sphere surface.

(ii). Nanocapsules are vesicular that the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane where the active substances are usually dissolved in the inner core but may also be adsorbed to the capsule surface

Nanocapsules can be different from other Nanoparticles because they have well defined core and shell, whereas the latter do not. When it is made from polymers, Nanocapsules can be referred as hollow polymer nanostructures<sup>1</sup>. Nanocapsules are extremely small, with sizes ranging from 10 nm to 1000 nm. Nano capsule have many potential medical applications in drug delivery, food industry, and nutraceuticals. The advantages of encapsulating techniques include pinpoint targeting, controlled release, and protection of these substances in harsh environments<sup>2</sup>.

## 2. ADVANTAGES OF NANOCAPSULES

- Nanocapsules are used as drug delivery systems by different ways of administrations such as oral and parental
- They reduce the toxicity of drugs
- They improve the stability of the drug.
- Nanocapsules are seen as active vectors because of their capacity to release drugs. Their subcellular size allows higher intracellular vectors.
- They can also improve the stability of active substances
- They have high drug encapsulation efficiency
- Polymeric shell provides protection against degradation of drug against different factors like pH and light
- They reduce tissue irritation<sup>3,4</sup>

The nanocapsule shells are formed by a wide variety of materials, such as polymers, lipids and phospholipids. Among these types of nanoparticles, polymer-based is one of the most promising nanostructures since they can provide high drug loadings, efficient protection against degradation, and high biocompatibility, considering the low tissue irritation and high interaction with biological fluids of some polymers<sup>5</sup>.

## III. POLYMERS

Polymers are large molecules composed of repeated chemical units. The smallest repeating unit is called a mer. The term polymer is derived from the Greek words *poly* and *mers* meaning "many parts. Polymers play a critical role in the preparation of nanocapsules. Polymers are generally classified as Natural polymers and synthetic polymers which is based on their source of origin<sup>6</sup>.

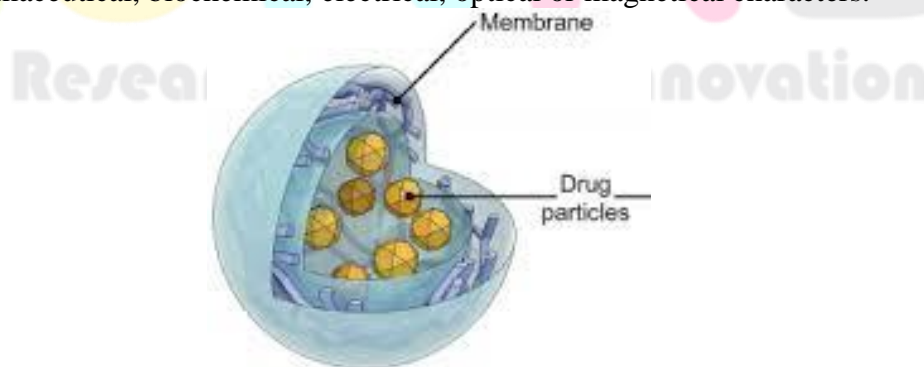
### a. Natural polymers

Natural polymers such as proteins, enzymes, muscle fibres, polysaccharides, and gummy exudates are used to make a wide range of pharmaceutical medicines. They include chitosan, carrageenan, pectin, acacia, agar, gelatin, shellac, guar gum, and gum karaya. These natural polymers are widely employed in pharmaceutical sectors as emulsifying agents, adjuvants, and packaging adhesives.

### b. Synthetic polymers

These are polymers that are created by humans. From the utility point of view they can be divided into four main categories viz., thermoplastics, thermosets, elastomers and synthetic fibers. A wide variety of synthetic polymers are available with variations in main chain and side chains. The back bones of common synthetic polymers such as polythene, polystyrene and poly acrylates are made up of carbon- carbon bonds, whereas hetero chain polymers such as polyamides, polyesters, polyurethanes, polysulfides and polycarbonates have other elements (e.g. oxygen, sulfur, nitrogen) inserted along the backbone.<sup>7</sup>

Nanocapsules, which are extremely small. The medicine is inserted into a hollow in a liquid or solid core, which is encircled by a unique polymer membrane composed of either natural or synthetic polymers. The protective layer of the nanocapsules, which is readily oxidised, has generated a lot of curiosity. Numerous nanometer-sized drug carriers have been developed. When a polymeric wall made of macromolecules, phospholipids, non-ionic surfactants, and an oil core is present, the polymeric nanocapsule is referred to as a nanocapsule. Two technologies are primarily used to prepare are interfacial polymerisation and interfacial nano deposition<sup>8</sup>. The production of nanocapsules depends on their application and pharmaceutical, biochemical, electrical, optical or magnetical characters.



**Figure 1: Structure of nanocapsules**

## IV. COMPOSITION OF NANOCAPSULES

The aqueous or organic phase of a nanocapsule, a submicroscopic colloidal drug carrier system, is encased in a thin polymer membrane. The membrane might be made of synthetic or natural polymers. The aqueous phase contains water and surfactants inside the membrane while the organic phase contains

solvent, polymer, oil, and medication. Two processes are used to prepare these nanocapsules: "interfacial deposition for polymers" and "interfacial polymerisation for monomers." The positively or negatively charged polymer will be introduced during the capsule preparation process. Every subsequent layer has been charged in the opposite direction from the one before it. They create the shells of poly electrolytes complex layers. It can form the capsule walls in 4-20 layers<sup>9</sup>.

## V. PROPERTIES OF NANOCAPSULES'

1. It is possible to create polymeric nanocapsules in the desired shapes, sizes, and in manageable amounts.
2. Nanocapsules can be engineered to perform many functions.
3. They can be produced like monodisperse particles with exactly defined biochemical, electrical, optical, and magnetic properties.
4. They can be tailored to suit the complexity of whatever application they are intended for, such causing the release of the contents in response to the particular bimolecular triggering mechanism in targeted drug-delivery systems<sup>10</sup>.

## VI. METHODS OF PREPARATION OF NANOCAPSULES

The preparation of nanocapsules can be different types as discussed below

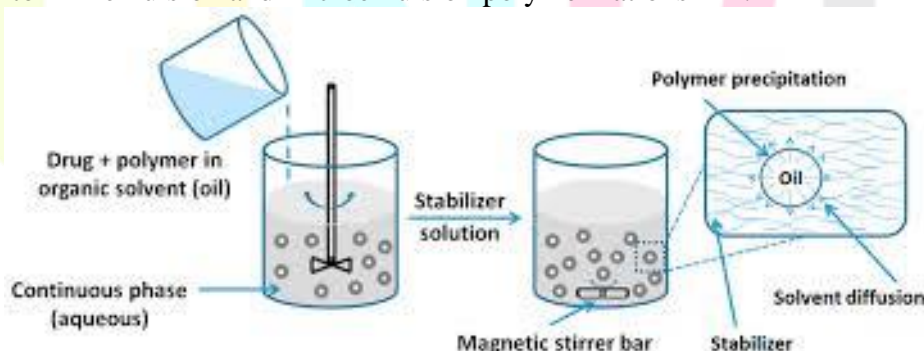
- a) Polymerisation method
- b) Emulsion polymerisation
- c) Interfacial polymerisation
- d) Miniemulsion Polymerization

### a) Polymerisation method

After the monomers are polymerised in an aqueous solution to create nanoparticles, the medicine is added either by adsorption of the nanoparticles or by dissolving in the polymerisation medium. The ultracentrifugation process, which has been used to purify the suspension of nanoparticles, eliminates different stabilisers and surfactants used in polymerisation. After that, the nanoparticles are resuspended in a media free of isotonic surfactants. It has been proposed for the production of nanoparticles of polybutylcyanoacrylate or polyalkylcyanoacrylate. The concentration levels of surfactants and chemical and physical stabilisers used determine the production of nanocapsules and the size of their particles. A mean diameter range of 20 nm to 100 nm is suggested by the formulation of the nanoparticles based on the phase-inversion technique<sup>11</sup>.

### b) Emulsion polymerisation method

The emulsion polymerization method for preparing nanocapsules is based on modifying traditional emulsion polymerization, where monomers are dispersed in water to form an emulsion with the aid of an emulsifier and mechanical stirring. Then, an initiator is added to trigger the polymerization of the monomers. The principle of emulsion polymerization in preparing nanocapsules is that the core material, surfactant, emulsifier, and polymer monomer are dispersed as tiny droplets to form an emulsion at the nanoscale. The polymer monomer can also be present in the mobile phase, which then triggers a polymerization reaction to produce a polymer to coat the core material to make nanocapsules. Depending on the thermodynamic stability of the emulsion, emulsion polymerization for nanomicrocapsules can be divided into miniemulsion and microemulsion polymerizations<sup>12, 13</sup>.

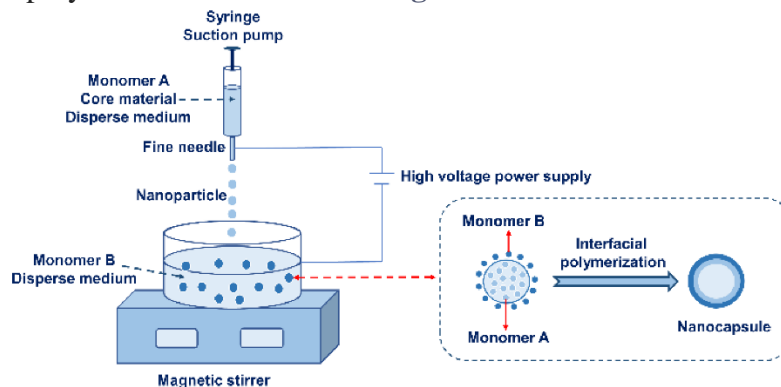


**Figure 2. Schematic representation of emulsion polymerisation method**

### c) Interfacial polymerization

This method is often applied to the preparation of microcapsules, requiring polymer monomers to move toward the interface either by their own or external forces. This triggers a polymerization reaction at the interface of the two phases to produce a polymer-coated core. However, interfacial polymerization at the nanoscale requires more precise manipulation. Two monomers containing double (multiple) functional groups are dissolved separately in two different liquids using interfacial polymerization. Then, the polycondensation reaction will occur at the two-phase interface. A fine needle syringe with capillaries is generally used to obtain nano-sized capsule particles. The core

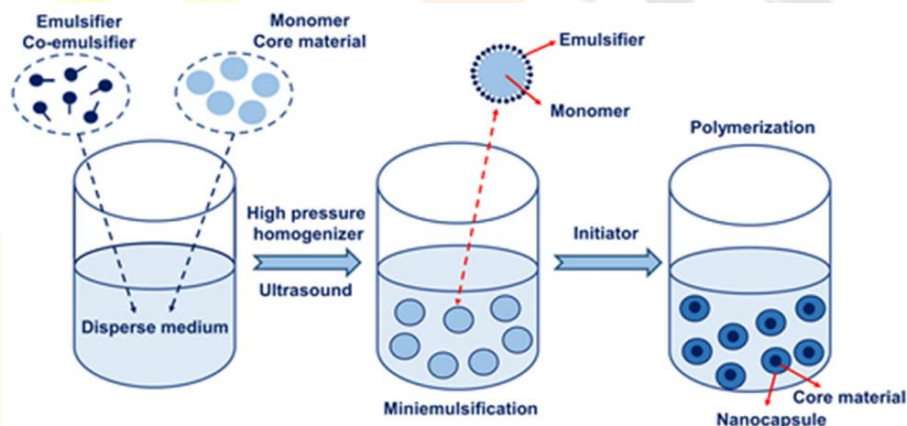
material solution and one monomer solution are added to the syringe, then the syringe needle is placed close to the liquid surface of the other monomer solution, and a high-voltage direct current is applied between the needle and the liquid surface. A high-voltage electric field drives the liquid in the syringe to form a uniformly spherical droplet (the particle size is in the nanometer scale) with a surface charge, which is dropped into the second monomer solution. At this time, the two polymerization monomer kinds move from the inside of the two phases to the interface of the droplets and react rapidly at the interface of the two phases to form polymers. The core material is coated by the polymer to form nanocapsules<sup>14, 15</sup>. A schematic diagram of preparing nanocapsules using interfacial polymerization is shown in **Figure 3**.



**Figure 3. Schematic representation of preparation of nanocapsules by interfacial polymerisation**

#### e) Miniemulsion Polymerization

Recent advances in the encapsulation technology has been utilized to formulate micro/nanocapsules with their explicit application properties used in food, biology, and medicine. Most encapsulation technique employ isocyanates in either solvent or bulk to construct shell, or making pressure on sensitive copying paper. Encapsulation delays the release of drug from nanocapsules, e. g., Xerogels and Aerosil 200 that are used as encapsulated materials. The Aerosil 200 has the strong drawback as bursting the nanocapsules. To diminish the burst release of drugs from xerogel mesopores, different strategies have been proposed<sup>16</sup>.



**Figure 4. A schematic diagram of the preparation of nanocapsules via miniemulsion polymerization.**

Different other methods viz., layer-by-layer self-assembly technology, nanoprecipitation, supercritical fluid, and nano spray drying are also used to prepare nanocapsules which are out of scope of this article<sup>17</sup>.

## VII. EVALUATION AND CHARACTERISATION OF NANOCAPSULES

Nanocapsules are generally tested for following parameters

#### a) Particle size

Particle size and size distribution plays a crucial role in nanocapsule systems and it establishes the in vivo distribution, bioavailability, toxicity and the targeting capacity of nanoparticulate systems. It also quite often influences the capacity of drug loading, drug release and the stability of nanoparticulate systems. Depend on the particle size the effect of releasing dosage and the time lapse of pharmacological action is the basis. The smaller particles have greater surface area; therefore, most of the therapeutic agents associated at or near to the surface particle, lead to instant drug release, whereas, the larger particles having the large core surfaces gradually diffuse out.<sup>88</sup> Particle size can also affect the polymer degradation. Photon correlation spectroscopy or dynamic light scattering are used to determine the particle size<sup>18</sup>.

#### b) Determination of pH

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

### c) **Surface characteristics**

Given the use of nanocapsules for drug targeting, this is followed by

- (a) coating the nanocapsules' surface with hydrophilic polymers and/or hydrophilic surfactants, and
- (b) creating nanocapsules using biodegradable copolymers of hydrophilic segments such as poly-ethylene glycol (PEG), poly-ethylene oxide (PEO), poly-oxamer, poly-xamine, and poly-sorbate 80 (Tween 80).

The charge on the surface of the nanocapsule can be effectively characterised using its zeta potential. Essential for extending their circulation in vivo and reducing opsonisation and lengthen their circulation in vivo<sup>18</sup>.

### d) **Determination of drug content**

Drug content was determined by dissolving 1ml of prepared nanocapsules in 20ml of suitable solvent. Appropriate quantity of sample was then subjected to the UV Spectrophotometer suitable wavelength. The absorbance for each sample was measured and compared with the Standard<sup>19</sup>.

### e) **In-Vitro release**

*In vitro* dissolution studies were carried out using USP type II dissolution Apparatus. The study was carried out in 100 ml 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  $37 \pm 0.5$  °C. The stirring rate was maintained at 100 rpm. At predetermined time Intervals 5ml of sample were withdrawn and is used to estimate the drug release by suitable method. After each withdrawal 5 ml of fresh dissolution medium was added to dissolution basket<sup>18,19</sup>.

### f) **X-Ray Diffraction (XRD) studies**

X-ray spectroscopy measurements are performed on suitable equipment with a monochromatic X-ray source (an aluminium K $\alpha$  line of 1486.6 eV energy and 150 W) to describe the valency of surface aluminium atoms present on the nanocapsules at a depth of 1.6 nm. This technique is highly specific to the solid surface due to the narrow range of photoelectrons that are excited. The excited energy of the photoelectrons emitting from the sample is determined by using a concentric hemispherical analyzer (CHA) which demonstrates a spectrum with a serial levels of the photoelectron peaks. The binding energies of the peaks are characteristic to each element. The peak areas are utilized (with equivalent sensitivity factors) to demonstrate the composition of the surface materials. The shape of each peak and binding energy can be slightly varied by the emitting atom of chemical state. XPS technique provides the chemical bonding information as well<sup>20</sup>.

### g) **Scanning Electron Microscopy (SEM)**

The architecture of the hierarchical branching aggregates, characterized from nanocapsules, may be of flocculent structure, small clusters, big clusters and big branches step by step at different scales, which confirms the self-similar attributes of the structure. It is characterized by a Philips XL-30 scanning electron microscope (SEM) which shows at a high magnification the clear morphology of small clusters. The clusters are composed of flocculent structure formed by the small particles adhered together. A low magnification SEM image may reveal the coral-like architecture that contains hierarchical branching characteristics along the axial and lengthwise directions<sup>20</sup>.

### h) **Differential Scanning Calorimetry (DSC)**

DSC analysis is conducted in both open samples (no lid) and closed samples (pan capped possessing a small hole in the center). Both methods have similar thermal behavior as per the observations reported<sup>21</sup>.

### i) **Transmission Electron Microscopy (TEM)**

The transport of particularly insulin-loaded nanocapsules across the epithelium can be assessed by transmission electron microscopy after their oral administration to experimental rats when they are subjected to in vitro and in vivo studies. TEM observations indicate the intestinal absorption of biodegradable nanocapsules leading to the transport of insulin across the epithelium mucosa<sup>22</sup>.

### j) **FT-IR analysis**

The presence of characteristic peaks is confirmed by using the FTIR analysis. The peaks indicate the characteristic functional groups of compound<sup>23</sup>.

## VIII. APPLICATIONS<sup>24,25</sup>

### a) **Nanocapsule for drug delivery**

Nanocapsules, which measure 1 thousandth of a millimeter, can be coated with an antibody on the surface,

which assists in directing them from the blood stream to an induced tumor. After reaching to the tumor, an instant Blast occurs that makes the capsules to open up and Discharge their therapeutic contents. On the surface of the polymer, there are tiny gold particles in the range of 6 nm i.e. 6 millionth of a millimeter which stick across and are specific to the laser light and lead the capsules to position their drug load capacity at the desired time .

#### b) **Nanocapsule as 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.

#### c) **Food science and agriculture**

Liposomes, spherical bilayer vesicles from dispersion of polar lipids in aqueous solvents, have been widely studied for their ability to act as drug delivery vehicles by shielding reactive or sensitive compounds prior to release. Liposome entrapment has been shown to stabilize encapsulated, bioactive materials against a range of environmental and chemical changes, including enzymatic and chemical modification, as well as buffering against extreme pH, Temperature, and ionic strength changes .

#### D) **Nanocapsule for self-healing materials**

Damage in polymeric coatings, adhesives, microelectronic components, and structural composites can span many length scales. Repair of large-scale damage (e.g. a projectile or blast is difficult and, when possible, requires use of bonded composite patches over the effective area 8. For smaller scale crack damage, However, a novel method of autonomic repair has been achieved through the use of self-healing polymers microcapsules that contain the healing agent must possess adequate strength, long shelf-life, and excellent bonding to the host material.

#### e) **New cancer weapon-nuclear nanocapsule**

The radioactive compound Astatine, like radium and uranium, emit high velocity alpha particles by the procedure of radioactive decay, which is about 4,000 Times faster than the beta decay of the emitted electrons, and is most commonly used to treat cancer. The unique combination of the low penetrating power as well as large particle size make the alpha particle unique for Targeting tumor at the single cellular level .

#### f) **Future nanocapsule bandages to fight infection**

The conventional dressings require to be taken out if the Skin becomes affected or it slows the healing. In contrast, nanocapsular dressings trigger automatically to discharge antibiotics when the wound becomes infected. They do not require to be removed, Thereby enhancing the chances of healing wound without Scarring . Nanocapsular bandages can also be used for Additional types of wounds like ulcers and most consistently by the military people on the battlefield. These Medicinal dressings' release antibiotics from the nanocapsules activated by the presence of disease causing Pathogenic or causative bacterial organism, targeting the Treatment prior to the infection aggravates. The bacterial Toxins burst the capsules comprising the antibiotics, which cover as the dressings .

### IX. **FUTURE BENEFITS, OPPORTUNITIES AND CHALLENGES OF NANOCAPSULES** <sup>26</sup>

Benefits: The nanocapsules have the ability to deliver existing drugs to their target. Nanocapsules should allow as much as a 10,000 fold decrease in drug dosages, reducing the harmful side effects of drug used in chemotherapy. There are many challenges can exist for developing the techniques like Architecting of biomimetic polymers, control of sensitive drugs, functions of active drug targeting, bioresponsive triggered systems, systems interacting with smart delivery, delivery of proteins drug delivery techniques, to deliver or control the rate & amount of drug delivery.

### X. **CONCLUSION**

Through a variety of techniques, primarily interfacial polymerisation and interfacial nano-deposition, Nanocapsules contribute to the formulation of methodological development. They can also be released as monodisperse particles with distinct optical, electrical, magnetic, and biological characteristics. In the fields of biochemistry, pharmacology, electronics, and molecular diagnostics, nanomaterials have found numerous significant uses. Their great repeatability and broad range of applications stem from their micronised size, making them suitable for use in life science applications. Nanocapsules are effectively used in a variety of fields, including waste water treatment, cosmetics, agrochemicals, genetic engineering, and cleaning goods. Enzymes, organic or inorganic catalysts, oil nanoparticles, adhesives, surface polymers, and even biological organisms can all be encapsulated with them. It is possible to use nanocapsules as smart drugs.

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