



NANOCAPSULES: A MULTIFACETED APPROACH TO DRUG DELIVERY AND THERAPEUTIC INNOVATION

Kiran C. Mahajan^{1*}, Aditya R. Suryawanshi¹, Neha B. Said¹, Nikita C. Wavhal², Krupa A. Khadakban¹, Ruchita L. Kharik¹, Najiya J. Tmboli¹

¹Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist.- Pune, Maharashtra, India, 410504.

²Department of Pharmacology, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist.- Pune, Maharashtra, India, 410504.

Corresponding Author: Dr. Kiran C. Mahajan*

Professor, Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist.- Pune, Maharashtra, India, 410504

ABSTRACT:

Aim: To clarify the various kinds, production processes, and uses of nanocapsules, with an emphasis on their use in targeted treatments, particularly in oncology.

Objective: To emphasize the benefits of nanocapsules, such as their capacity to encapsulate a variety of therapeutic substances, produce regulated release profiles, and enable surface functionalization for improved targeting.

Purpose: It illustrate how the choice of polymers and creative production techniques help to maximize the drug delivery, scalability, and reproducibility of nanocapsules.

Discussion: Highlights the necessity of using both natural and synthetic polymers to optimize medication administration, as well as the value of using cutting-edge production techniques like coacervation and spray drying. focuses on issues pertaining to safety evaluations and adherence to regulations for clinical translation.

Conclusion: Drug delivery could be revolutionized by the continued development of nanocapsules, which is being fueled by advances in materials science and technology. For better clinical results, future research should concentrate on improving functionality, investigating new materials, and incorporating intelligent delivery systems.

KEYWORDS: Drug delivery systems, Targeted therapeutics, Polymer selection, Controlled release, Oncology.

INTRODUCTION:

Nanoparticles are solid colloidal particles that typically range in size from 5 to 1000 nm, with the majority falling between 100 and 500 nm. This includes both nanospheres and nanocapsules. The amazing capacity of these nanoparticulated systems to improve treatment outcomes and enhance



drug release has made them promising dynamic drug delivery vectors. When compared to conventional particle systems, their subcellular diameters result in superior intracellular absorption, provide improved stability for active pharmaceutical ingredients (APIs), and guarantee biocompatibility when made from biodegradable or biocompatible materials. Because of these properties, nanoparticles are a useful tool in the fields of controlled release systems and targeted medication delivery.

As drug carriers, nanoencapsulated systems provide unique benefits over other forms of nanoparticulated systems. Their high drug encapsulation effectiveness, which is attained by improving solubility within the nanocapsule's core, is one of its main advantages. Furthermore, these systems require less polymer than other nanoparticulated systems, which can help minimize potential toxicity connected to polymers. By keeping drug levels within the therapeutic window for extended periods of time, the possibility of controlled and sustained release of medications further improves their therapeutic efficacy¹.

One extensively researched nanoplatform that has the potential to greatly impact the pharmacokinetics and biodistribution of encapsulated medications is polymeric nanoparticles. The distribution of medications within polymeric nanoparticles is mostly controlled by the physicochemical characteristics of the carrier system, as opposed to free pharmaceuticals, which tend to spread widely across tissues and organs. By concentrating the medicinal drug at the intended site of action, this targeted delivery method enhances efficacy and lowers systemic side effects. These systems are made more versatile by the ability to modify drug release profiles by changing the particle size and polymer composition.

As a subclass of polymeric nanoparticles, nanocapsules have a core-shell structure in which a polymeric shell envelops a liquid or solid core. The stability and shelf life of the encapsulated medication are improved by this special architecture, which is made of natural or synthetic polymers and offers a barrier against environmental elements including oxidation. By adjusting its permeability to the medicine it encapsulates, the polymeric shell not only provides protection but also enhances the nanocapsule's controlled release capabilities. Oral, parenteral, and topical administration routes are only a few of the pharmacological applications in which these systems have proven useful. Nanocapsules have made it possible to create safer and more potent medicinal formulations by lowering medication toxicity and improving stability^{2, 3}.

The development of nanocarrier systems has advanced significantly over the last fifty years. Specifically, polymeric nanocapsules are distinguished by their polymeric walls made of oil cores, macromolecules, phospholipids, and non-ionic surfactants. Both hydrophilic and hydrophobic



medications can be encapsulated using these components, which add to the versatility of nanocapsules. By lowering surface tension and inhibiting aggregation, the use of non-ionic surfactants improves the stability of the nanocapsules, which is essential for preserving a steady and predictable drug release profile.

Additional advantages of using natural polymers such chitosan, alginate, and gelatin in the production of nanocapsules include their inherent bioactivity, low toxicity, and biodegradability. Poly(lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL) are examples of synthetic polymers that offer improved control over the mechanical strength and rate of degradation of the nanoparticles. The physical characteristics of the nanocapsules, such as size, surface charge, and drug release kinetics, are greatly influenced by the polymer selection and production technique. One flexible and very successful nanoplatform for drug delivery is polymeric nanocapsules. They are essential to the creation of next-generation medications because of their capacity to encapsulate a variety of therapeutic substances, as well as their improved stability and controlled release characteristics. In order to better optimize these systems and achieve even more accuracy in targeted drug delivery and therapeutic efficacy, ongoing research is still looking at novel materials and creative ways^{4,5}.

TYPES OF NANOCAPSULES:

Based on their composition, structure, and surface characteristics, nanocapsules are a flexible and sophisticated family of nanocarriers. These categories affect their effectiveness in drug transport, targeting, and therapeutic efficacy in addition to directing their selection for certain pharmaceutical applications. Each of the four main categories of nanocapsules polymeric, lipid-core, inorganic, and hybrid offers unique benefits and difficulties for use in biomedical applications⁶.

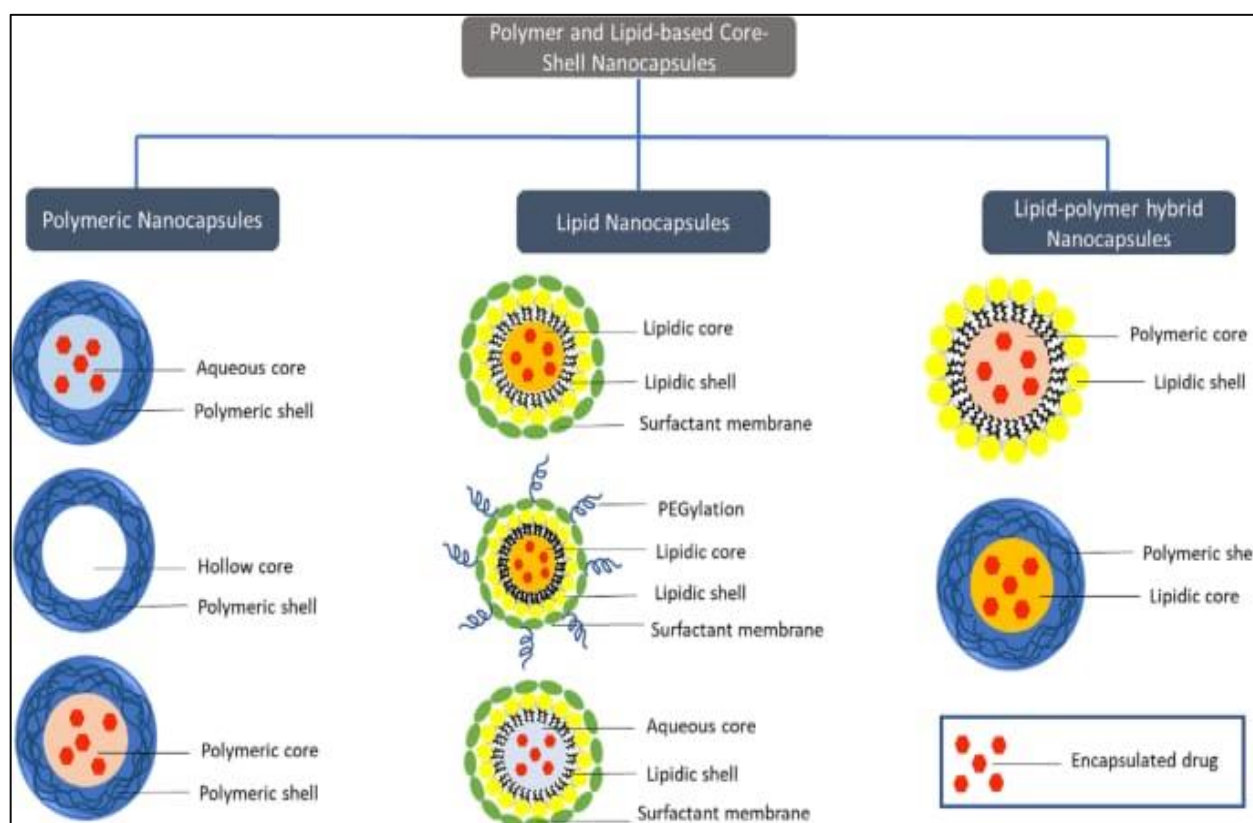


Figure 1: Schematic representation of polymer and lipid-based core-shell nanocapsules

The diagram illustrates the structural diversity of nanocapsules, categorized into polymeric, lipid, and lipid-polymer hybrid types. Key components such as the aqueous core, polymeric shell, lipidic core, lipidic shell, surfactant membrane, and encapsulated drug are highlighted. The inclusion of PEGylation in lipid nanocapsules is also shown.

1. Polymeric Nanocapsules:

Since polymeric nanocapsules may transport a variety of therapeutic compounds and are biocompatible and biodegradable, they are one of the most researched types of nanocarriers. Usually, these nanocapsules are made of synthetic polymers like poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), and polyethylene glycol (PEG) or natural polymers like chitosan, alginate, and gelatin. In addition to providing structural stability, the polymeric shell regulates the encapsulated drug's release profile by altering the polymer matrix's permeability and rate of breakdown. Furthermore, surface changes of polymeric nanocapsules can be tailored to optimize pharmacokinetics, decrease immunogenicity, and increase targeted specificity. The attachment of ligands, antibodies, or peptides that promote receptor-mediated endocytosis at the target location is frequently a part of these alterations⁷.

2. Lipid-Core Nanocapsules:



Lipid-core nanocapsules combine the advantages of polymeric and lipid-based nanocarriers by enclosing a lipid core in a polymeric shell. In order to improve the solubility and bioavailability of weakly water-soluble medications, the hydrophobic lipid core is very useful for encapsulation. In addition to stabilizing the lipid core, the polymeric shell offers a surface modification platform that enhances target selectivity and biocompatibility. In the delivery of chemotherapeutic drugs, where regulated and prolonged drug release is essential for reducing side effects and improving therapeutic outcomes, lipid-core nanocapsules have shown great promise. Furthermore, these nanocapsules' lipid component frequently resembles biological membranes, which promotes cellular uptake and lessens cytotoxicity⁸.

3. Inorganic Nanocapsules:

Materials including silica, metal oxides (such as iron oxide and titanium dioxide), and gold nanoparticles are used in inorganic nanocapsules. The multifunctionality of these nanocapsules, which provide imaging and diagnostic applications in addition to drug delivery capabilities, makes them especially important. Iron oxide-based nanocapsules, for instance, can deliver therapeutic drugs to the target site while also acting as contrast agents in magnetic resonance imaging (MRI). Inorganic nanocapsules are appropriate for applications requiring extended circulation durations because of their stiff structure, which also offers stability in challenging physiological conditions. To guarantee safety in clinical applications, it is necessary to carefully evaluate the biodegradability and possible toxicity of inorganic materials^{9,10}.

4. Hybrid Nanocapsules:

Organic and inorganic components are combined in hybrid nanocapsules to produce multipurpose drug delivery systems with improved therapeutic efficacy. These methods create nanocarriers with enhanced stability, controlled release, and targeted delivery capabilities by combining the imaging or therapeutic qualities of inorganic cores with the biocompatibility of polymeric shells. In theranostic applications, where simultaneous drug delivery and imaging allow for real-time treatment efficacy monitoring, hybrid nanocapsules are very helpful²⁸. Furthermore, these nanocapsules can be designed to react to external stimuli like temperature, pH, or magnetic fields, providing site-specific and controlled drug release¹¹.

5. Protein-Based Nanocapsules:

Albumin, gelatin, or silk fibroin are examples of natural proteins that are used to create protein-based nanocapsules. These proteins have intrinsic biological activity, biocompatibility, and biodegradability, all of which can improve treatment results. For instance, because albumin-



based nanocapsules can take advantage of the increased permeability and retention (EPR) effect in tumor tissues, they have been employed extensively in anticancer therapy. To increase selectivity and lessen off-target effects, targeting moieties can also be functionalized into the protein shell¹².

6. Dendritic Nanocapsules:

Dendrimers, which are highly branched, tree-like polymers that offer a vast surface area for drug loading and functionalization, are incorporated into dendritic nanocapsules. The size, shape, and surface chemistry of these nanocapsules may be precisely controlled, all of which are important factors in cellular absorption and biodistribution. Multiple ligands can adhere to the multivalent surface of dendritic nanocapsules, facilitating targeted administration and improved cell receptor engagement. Additionally, the internal holes of dendrimers offer a hydrophobic environment that can be used to encapsulate a variety of therapeutic substances, such as biologics and small compounds¹³.

7. Polysaccharide-Based Nanocapsules:

Natural polysaccharides like chitosan, dextran, and hyaluronic acid are used in polysaccharide-based nanocapsules. These materials are perfect for biomedical applications because they have low toxicity, high biocompatibility, and biodegradability. For instance, chitosan-based nanocapsules have mucoadhesive qualities that improve medication distribution across mucosal tissues, such as the respiratory and gastrointestinal systems. Furthermore, for targeted medication administration, especially in cancer and inflammatory illnesses, the inherent affinity of certain polysaccharides for particular cell receptors can be used¹⁴.

MANUFACTURING OF NANOCAPSULES:

Nanocapsules are made using a variety of sophisticated procedures, each of which has unique benefits in terms of particle size control, encapsulation efficiency, and compatibility with diverse active chemical types. The active ingredient's physicochemical characteristics, the intended use, and the required release profile all influence the technique selection. Spray drying, addition complexation, rotational or centrifugal separation, extrusion, fluidized bed coating, liposome entrapment, and coacervation are a few of the most popular fabrication techniques¹⁵⁻¹⁷.

1. Spray Drying:

For the manufacture of nanocapsules, spray drying is a flexible and popular technique, especially in the food and pharmaceutical sectors. A solution or suspension including the active



component and the carrier material is atomized and then placed in a heated chamber, where quick solvent evaporation causes dry particles to form. Due to its excellent encapsulation effectiveness and gentle processing conditions, this method is especially useful for encapsulating heat-sensitive substances including flavors, vitamins, and probiotics. Furthermore, spray drying is a popular option for industrial applications due to its scalability¹⁸⁻²⁰.

2. Addition Complexation:

In order to create inclusion complexes with hydrophobic molecules, addition complexation uses β -cyclodextrin or other cyclodextrin derivatives. The solubility, stability, and bioavailability of weakly water-soluble substances, such as fat-soluble vitamins and essential oils, can be improved with this technique. A regulated release profile for the encapsulated medicine is provided by the spontaneous creation of host-guest complexes through non-covalent interactions during the encapsulation process. Furthermore, in nutraceutical formulations, β -cyclodextrin-based nanocapsules have demonstrated promise in masking disagreeable tastes and odors²¹.

3. Rotational or Centrifugal Separation:

An developing method for producing nanocapsules is rotational or centrifugal separation, which uses centrifugal force to accomplish encapsulation. This process involves rotating a mixture of core and wall materials at high speeds, which causes phase separation and the creation of nanocapsules. This method provides exact control over capsule size and homogeneity and is beneficial for encapsulating a wide range of active components, including hydrophilic and hydrophobic substances. This technique is also appropriate for heat-sensitive materials since it is less reliant on solvent conditions and temperature²².

4. Spray Cooling:

Spray chilling, sometimes referred to as spray congealing, is the process of emulsifying the active component and then quickly cooling it to create solid particles. This technique is frequently employed to encapsulate lipophilic substances and holds great promise for controlled-release formulations in the pharmaceutical sector. The encapsulating substance is solidified during the cooling process, producing stable nanocapsules with a distinct core-shell structure. For the production of nanocapsules with high drug loading and stability against oxidation and environmental degradation, spray cooling is very advantageous²³.

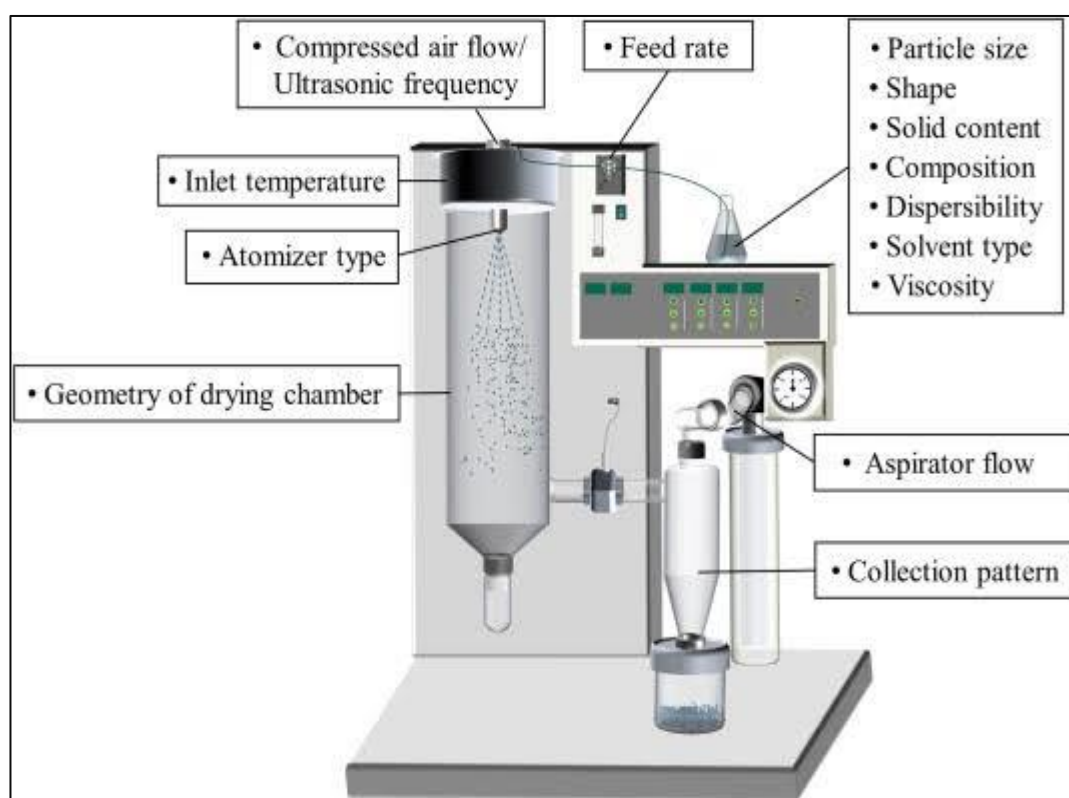


Figure 2: Schematic diagram of a typical spray dryer apparatus

The illustration depicts the key components of a spray dryer, highlighting parameters influencing the process and resulting particle characteristics. These include inlet temperature, atomizer type, compressed air flow/ultrasonic frequency, feed rate, geometry of the drying chamber, aspirator flow, and collection pattern. Particle properties influenced by these parameters include particle size, shape, solid content, composition, dispersibility, solvent type, and viscosity.

5. Extrusion:

Extrusion methods are used to create homogeneous nanocapsules with regulated particle size and distribution, such as membrane extrusion and self-emulsification. The core material is



pushed through a nozzle or membrane in this procedure, where it combines with the encapsulating polymer to create nanocapsules. Proteins, peptides, and nucleic acids are examples of sensitive bioactive substances that benefit greatly from the method's high repeatability. To improve encapsulation efficiency, extrusion can also be used in conjunction with other methods such solvent evaporation or nanoprecipitation²⁴.

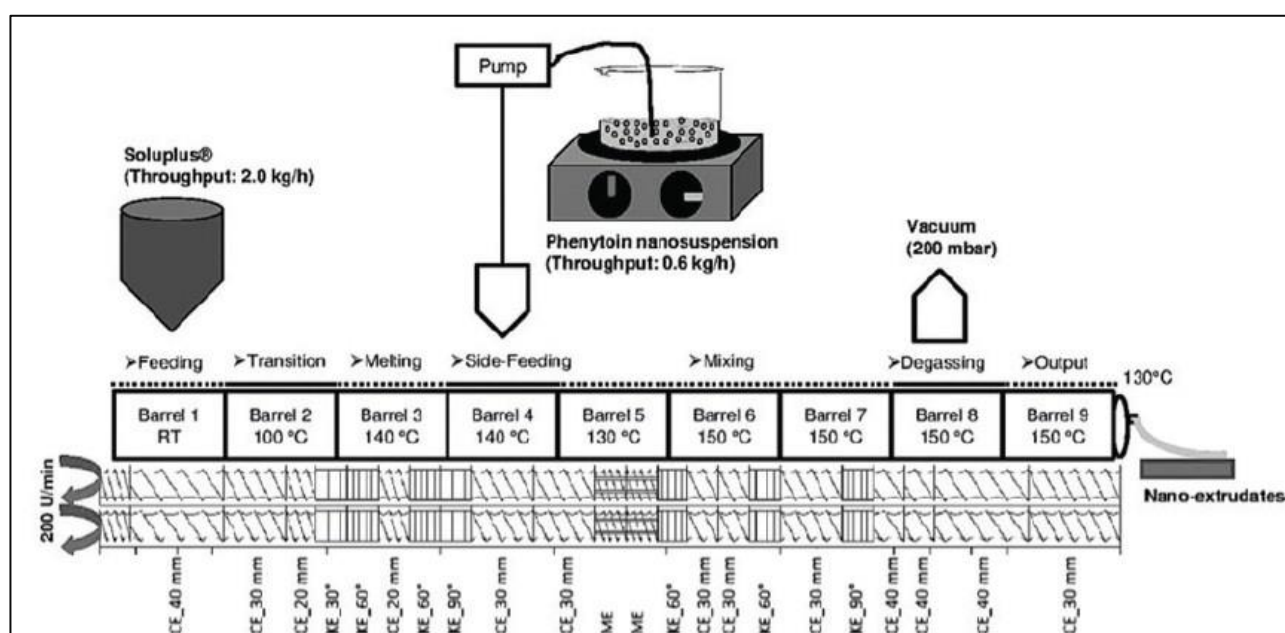


Figure 3: Schematic representation of the hot-melt extrusion (HME) process for nano-extrudate production

The diagram illustrates the twin-screw extruder setup, including the feeding of Soluplus® and phenytoin nanosuspension. The extruder consists of nine barrels with controlled temperature zones to facilitate feeding, transition, melting, side-feeding, mixing, and degassing, before the final output of nano-extrudates. Screw elements are displayed to demonstrate their position. Processing parameters are indicated, including throughput rates, screw speed, barrel temperatures, and vacuum pressure.

6. Fluidized Bed Coating:

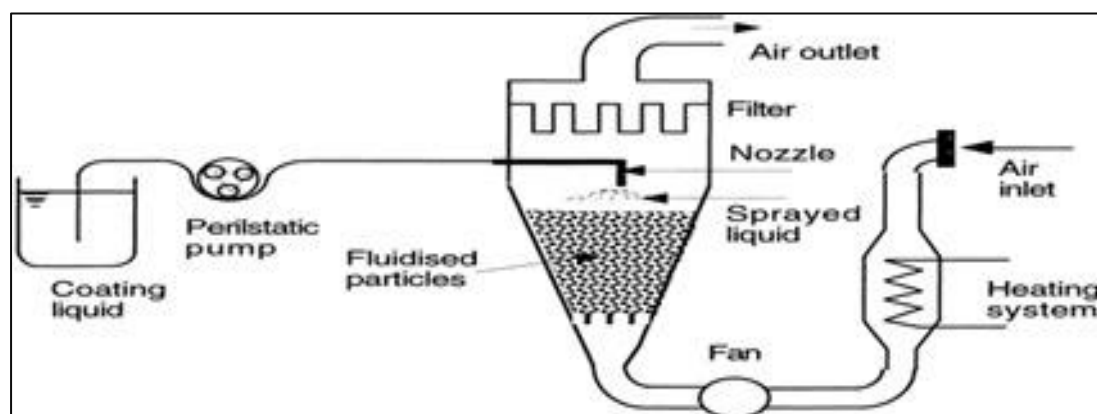


Figure 4: Fluidized bed coating process

The schematic illustrates the key components of a fluidized bed coating system. The coating liquid is delivered via a peristaltic pump to a nozzle, where it is sprayed onto fluidized particles. Air enters through an air inlet, is heated, and then passed through the bed of particles, causing them to fluidize. Exhaust air exits through an air outlet and a filter system to capture any entrained particles.

A one-step encapsulation technique called fluidized bed coating is mostly utilized to produce lipid-core nanocapsules that can be taken orally. This method creates a uniform coating by suspending particles in an upward air flow and spraying a coating material onto their surface. This method is very useful for increasing granule redispersibility and encapsulated component stability in gastrointestinal environments. Furthermore, enteric coatings and other functional layers can be applied using fluidized bed coating to accomplish tailored medication release in the colon²⁵.

7. Liposome Entrapment:

Liposome entrapment is the process by which lipid bilayers encircle the active component to form liposomes, which are vesicular nanocapsules. To produce liposomes with the appropriate size and stability, energy input is needed through processes like sonication or extrusion. Both hydrophilic and lipophilic substances can be encapsulated via liposome entrapment, which provides a flexible platform for drug delivery and nutraceutical applications. Liposomes' biocompatible phospholipid bilayer can merge with cell membranes to improve bioavailability and cellular absorption²⁶.

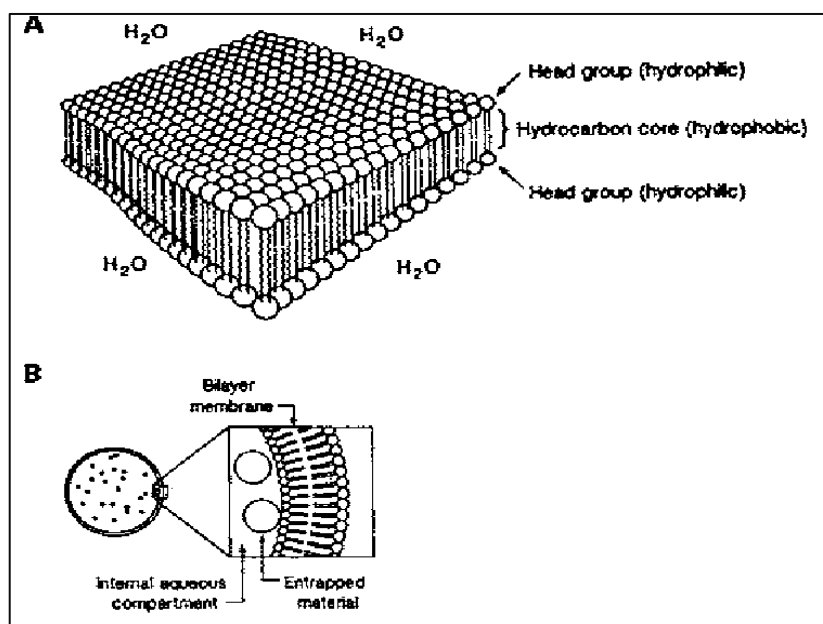


Figure 5: Structure of lipid bilayers and liposomes

(A) Schematic representation of a lipid bilayer, showing the arrangement of lipid molecules with hydrophilic head groups facing the aqueous environment (H₂O) and hydrophobic hydrocarbon tails forming the core. (B) Illustration of a liposome, consisting of a spherical bilayer membrane encapsulating an internal aqueous compartment containing entrapped material.

8. Coacervation:

Coacervation is a phase-separation method that produces nanocapsules by solvent-induced phase separation or the interaction of oppositely charged polymers. With its excellent encapsulation efficiency and regulated release characteristics, this technique works especially well for encapsulating both polar and non-polar active chemicals. The coacervation technique is appropriate for use in food, medicine, and cosmetics since it may be applied to a variety of materials, such as proteins, polysaccharides, and synthetic polymers. Additionally, coacervate nanocapsules can improve the stability of sensitive bioactive substances by acting as a barrier against environmental influences²⁷⁻³⁰.

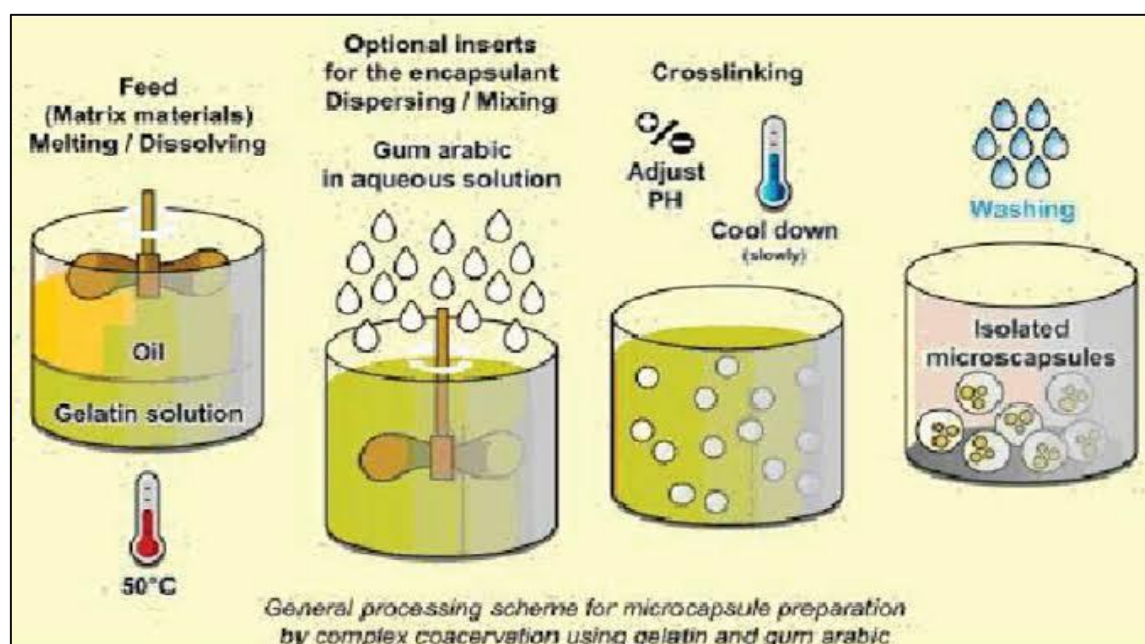


Figure 5: General processing scheme for microcapsule preparation by complex coacervation using gelatin and gum arabic

The schematic illustrates the key steps in the microencapsulation process. The process begins with melting or dissolving the matrix materials (oil in gelatin solution) in the feed stage, followed by the optional addition of gum arabic in aqueous solution for dispersing/mixing. The mixture undergoes crosslinking through pH adjustment and cooling, resulting in microcapsule formation. Finally, the microcapsules are washed and isolated.

EXCIPIENTS IN NANOCAPSULE FORMULATIONS:

Excipients are essential ingredients in nanocapsule formulations because they act as both functional agents and inert substances, greatly improving the drug delivery system's effectiveness. They support the encapsulated active pharmaceutical ingredients' (APIs') stability, bioavailability, release kinetics, and general effectiveness. Achieving the intended physicochemical characteristics of nanocapsules, including size, surface charge, and encapsulation efficiency, depends on the careful selection of excipients³¹.

1. Vitamins as Excipients



Vitamins are frequently used as excipients in nanocapsule formulations because they serve as both stabilizing agents and active components. To increase their stability, shield them from environmental deterioration, and boost their bioavailability, vitamins that are fat-soluble (such as vitamins A, D, E, and K) and water-soluble (like vitamins C and B-complex vitamins) are both encapsulated. Because they are hydrophobic, fat-soluble vitamins present special difficulties when it comes to encapsulation. A lipid or polymeric core that can solubilize these vitamins and improve their systemic availability and gastrointestinal absorption makes nanocapsule systems an efficient solution. For example, vitamin E-loaded lipid-core nanocapsules have shown enhanced antioxidant stability and controlled release characteristics, which are advantageous for applications in nutraceuticals and pharmaceuticals. Vitamins can also function as organic antioxidants, protecting other delicate bioactive substances inside the nanocapsule system. For instance, formulations frequently contain vitamin C to stop oxidative degradation of lipophilic medications that are encapsulated^{32, 33}.

2. Polymers in Nanocapsule Shell Formation

Nanocapsule shells are made of polymers, which give the encapsulated medications protection, controlled release characteristics, and structural integrity. Both natural and synthetic polymers fall within this category, and each has unique benefits for drug delivery systems³⁴.

3. Natural Polymers: Biodegradable, biocompatible, and frequently non-toxic, they include chitosan, alginate, gelatin, and cellulose derivatives. For example, chitosan improves mucoadhesive qualities, which prolongs residence duration at the site of absorption, especially in drug delivery via the mouth and nose. Because they may form hydrogels under physiological conditions, alginate-based nanocapsules are frequently utilized for the controlled release of hydrophilic medicines³⁵.

4. Synthetic Polymers: Common synthetic polymers used in nanocapsule formulations include poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), and polymethyl methacrylate (PMMA). PLGA is perfect for sustained-release medication formulations since it has FDA approval and provides controlled biodegradation. Because synthetic polymers are so adaptable, their surfaces can be altered to increase targeting, decrease immunogenicity, and lengthen circulatory circulation. Polymeric excipients can be functionalized with ligands for targeted drug delivery, such as folic acid for cancer cell targeting, and they can affect the mechanical strength of nanocapsules³⁶.

5. Surfactants as Stabilizing Agents



Because they lower surface tension and inhibit aggregation, surfactants amphiphilic molecules are essential for stabilizing nanocapsule formulations. To create homogeneous nanocapsules with a restricted size distribution, they help to create a stable emulsion during the construction process³⁷.

Typical surfactants include:

- i. **Non-ionic Surfactants:** For example, polysorbates (like Tween 80) and polyoxyl 35 castor oil (like Cremophor EL), which are extensively utilized because of their superior emulsifying qualities and low toxicity. By promoting the development of micellar structures, these surfactants increase the solubility and bioavailability of hydrophobic medications³⁸.
- ii. **Ionic Surfactants:** such as cetyltrimethylammonium bromide (CTAB) and sodium dodecyl sulfate (SDS), which give nanocapsules electrostatic stability. However, possible toxicity frequently restricts their use, especially in parenteral preparations³⁹.
- iii. **Natural Surfactants:** such as bile salts and lecithin, which are especially helpful in injectable and oral formulations and provide biocompatibility. Nanocapsules based on lecithin have demonstrated better cellular absorption and increased stability in biological fluids. Additionally, surfactants make it easier to functionalize the surface of the nanocapsule with polyethylene glycol (PEG) or targeted ligands for stealth characteristics, which decreases reticuloendothelial system (RES) recognition and lengthens circulation time⁴⁰.

EVALUATION OF NANOCAPSULE:

1. Determination of pH:

One important factor affecting the stability, drug release profile, and biocompatibility of nanocapsule suspensions is their pH. The ionization state of the polymeric shell and the encapsulated medication can be changed by pH variations, which may cause premature drug release or nanocapsule aggregation. A calibrated pH meter is usually used to monitor pH, and for biomedical purposes, it is frequently preferable to maintain a physiological pH. Additionally, pH-sensitive nanocapsules have been created for targeted medication release in particular situations, such the gastrointestinal system or the acidic conditions of tumor tissues⁴¹.

2. Determination of Drug Content:



The drug content is used to assess the encapsulation effectiveness and drug-loading capability of nanocapsules. Because of its great sensitivity, precision, and capacity to separate and measure the active pharmaceutical ingredient (API) from excipients and degradation products, great-Performance Liquid Chromatography (HPLC) is widely utilized. Maintaining a consistent dose and therapeutic efficacy requires precise drug content quantification. For certain medications, technologies such as Fluorescence Spectroscopy and Ultraviolet-Visible (UV-Vis) Spectroscopy are also used, providing faster and easier analysis procedures⁴².

3. Particle Size Distribution and Zeta Potential:

The stability, biodistribution, and cellular absorption of nanocapsules are critical properties that are influenced by their particle size and surface charge (zeta potential). The common method for determining the homogeneity and stability of nanocapsule suspensions is Dynamic Light Scattering (DLS), which measures the distribution of particle sizes. The surface charge of suspended particles, which reflects their electrostatic stability, is shown by the zeta potential. Because it lowers the chance of aggregation via electrostatic repulsion, a zeta potential above +30 mV or below -30 mV generally indicates high stability. The stability and interaction of nanocapsules with biological membranes can be improved by modifying the surface charge by adding surfactants or other surface modification techniques⁴³.

4. In Vitro Drug Release:

To mimic the encapsulated drug's release behavior under physiological settings, in vitro drug release experiments are carried out. The Dialysis Method is a widely utilized technique in which the medicine is allowed to diffuse over time by placing nanocapsules in a dialysis bag submerged in a release medium. By altering the encapsulating method or the polymer matrix, the release profile can be customized. It is possible to achieve sustained, regulated, or triggered release profiles, which are very helpful for sustaining therapeutic medication levels for prolonged periods of time. The release processes are analyzed using mathematical models as Higuchi, Korsmeyer-Peppas, and First-Order Kinetics⁴⁴.

5. X-Ray Photoelectron Spectroscopy (XPS):

An effective analytical method for examining the surface chemistry of nanocapsules is XPS. It offers comprehensive details on the surface materials' elemental makeup, chemical states, and electrical characteristics. This method is very helpful for verifying if targeted ligands or stabilizing agents have successfully functionalized the surface of nanocapsules. Understanding the interactions between the nanocapsule surface and the biological environment is crucial for



targeted and site-specific drug delivery systems, and it can be accomplished with the use of XPS data⁴⁴.

6. Scanning Electron Microscopy (SEM):

SEM provides high-resolution pictures of the structural properties and surface appearance of nanocapsules. A concentrated electron beam is used to scan the surface, creating fine-grained pictures that show the size, shape, and texture of the particles. SEM analysis can identify surface flaws or agglomerations and differentiate between spherical, rod-shaped, or irregular nanocapsules. SEM can also offer elemental composition analysis when paired with Energy-Dispersive X-Ray Spectroscopy (EDX), which improves comprehension of the material distribution inside the nanocapsules⁴⁵.

7. Superconducting Quantum Interference Device (SQUID):

SQUID is a cutting-edge method for assessing the magnetic characteristics of nanocapsules, especially those meant for magnetically targeted medication administration or magnetic resonance imaging (MRI). Even the smallest magnetic reactions from the nanocapsules can be detected by the technique's incredibly sensitive magnetic measurements. Using external magnetic fields, magnetic nanocapsules which frequently include iron oxide nanoparticles can be directed to certain locations within the body, improving the accuracy of drug delivery to target areas like tumors. Furthermore, the safety and efficacy of such theranostic applications depend heavily on the magnetic characteristics assessed by SQUID⁴⁵.

APPLICATIONS OF NANOCAPUSLES:

1. Nanocapsules for Medicine Delivery:

Nanocapsules, which are generally between 10 and 1000 nm in size, present a promising method for the targeted administration of medications. Nanocapsules can specifically target diseased areas, including tumors, by functionalizing their surfaces with certain antibodies. This reduces off-target effects and improves treatment efficacy. External stimuli, such as pH, temperature, or light, might cause the release of encapsulated medicines once they reach the target location, guaranteeing site-specific action.

The targeting capabilities of polymeric nanocapsules are improved by the incorporation of gold nanoparticles. For example, photothermal therapy for cancer treatment is made possible by these nanoparticles' ability to absorb light and transform it into heat. The gold nanoparticles produce localized heat when subjected to near-infrared (NIR) light, killing tumor cells while preserving nearby healthy tissues. For advanced oncological treatments, this approach is a prime example



of the synergistic potential of integrating nanotechnology with immunotherapy and radiotherapy⁴⁶.

2. Nanocapsules as Drug Delivery Systems:

Because polymeric nanocapsules offer focused delivery, extended circulation, and controlled release, they have completely changed drug delivery methods. Drugs are protected from enzymatic breakdown and their bioavailability is increased when they are encapsulated in polymeric nanocapsules. By adjusting the polymeric shell's composition and thickness, the drug's release profile can be precisely regulated. Poly(lactic-co-glycolic acid) (PLGA) is one example of a biodegradable polymer that permits a sustained release as it breaks down gradually inside the body. Furthermore, by decreasing identification and clearance by the reticuloendothelial system (RES), surface alterations employing polyethylene glycol (PEG) extend the circulation duration of nanocapsules⁴⁶.

3. Food Science and Agriculture:

In food science and agriculture, nanocapsules are being utilized more and more to improve the stability, bioavailability, and regulated release of nutrients and active ingredients. Vitamins, antioxidants, and essential oils can be effectively encapsulated in liposomes, a type of nanocapsule having a phospholipid bilayer. Precision farming in agriculture is made possible by nanocapsules, which offer controlled release herbicides, insecticides, and fertilizers. By lowering the quantity of chemicals released into the soil, this not only increases crop output but also lessens the impact on the environment. For instance, pesticides that are nanoencapsulated exhibit improved stability against environmental deterioration, guaranteeing that the active component will continue to be effective until it reaches the intended pest⁴⁶.

4. Nanocapsules for Self-Healing Materials:

Nanocapsules are utilized in materials science to create self-healing materials that can fix damage and microcracks on their own. These substances integrate microcapsules containing therapeutic agents (such as polyurethanes or epoxy resins) with polymeric coverings. The healing agent is released into the wounded area when the material cracks, rupturing the microcapsules. The healing agent polymerizes when exposed to external stimuli (such heat or UV radiation), successfully patching the crack and regaining the material's integrity¹¹⁴. In the construction, automotive, and aerospace sectors, where longevity and ease of maintenance are crucial, this technology is extensively used⁴⁶.

5. Nuclear Nanocapsules as Cancer Treatments:



Nuclear nanocapsules offer a novel way to treat cancer, especially when combined with radiation. Radioactive isotopes, like Astatine-211, which release alpha particles that can kill cancer cells with little harm to nearby healthy tissues, can be contained in these nanocapsules. The use of radioactive emulsions enables targeted radiotherapy, where nanocapsules accumulate specifically in tumor tissues. When they break down, radioactive particles are released, which starts localized radiation treatment. This technique improves the accuracy of oncological therapies and lessens the systemic toxicity frequently linked to conventional radiotherapy⁴⁷.

6. Future Nanocapsule Bandages to Combat Infection:

An advancement in wound treatment is represented by bandages embedded in nanocapsules. Regular dressing changes are no longer necessary because these bandages are made to release antibiotics automatically in response to infection. The pH-sensitive nanocapsules that contain the antibiotics react to the acidic environment that is usually found in infected wounds. The nanocapsules break down when harmful germs are found, releasing antibiotics at the infection site. This focused strategy encourages quicker healing and reduces the possibility of antibiotic resistance⁴⁸.

7. Application of Nanocapsules for Transdermal Drug Delivery Systems:

Transdermal drug delivery is a non-invasive technique that enables medications to enter the bloodstream through the skin. Drug penetration is improved by polymeric nanocapsules, which also lessen systemic side effects and increase therapeutic efficiency. When it comes to skin penetration, nanocapsule size is quite important. Research shows that when compared to larger particles, nanocapsules smaller than 100 nm have noticeably better penetration. When it comes to transporting hydrophobic medications through the stratum corneum, lipid-based nanocapsules such as solid lipid nanoparticles and nanoemulsions are very successful⁴⁹.

EXAMPLES OF MARKETED NANOCAPSULES:

Product Name	Active Ingredient	Indication	Nanocapsule Type	Manufacturer
Abraxane®	Paclitaxel	Breast, lung, and pancreatic cancer	Polymeric nanocapsule	Celgene Corporation
Doxil®	Doxorubicin	Ovarian cancer, multiple myeloma	Liposomal nanocapsule	Johnson & Johnson



Marqibo®	Vincristine sulfate	Acute lymphoblastic leukemia	Liposomal nanocapsule	Spectrum Pharmaceuticals
Onivyde®	Irinotecan	Metastatic pancreatic cancer	Liposomal nanocapsule	Ipsen Biopharmaceuticals
Ambisome®	Amphotericin B	Fungal infections	Liposomal nanocapsule	Gilead Sciences
DepoDur®	Morphine sulfate	Pain management	Liposomal nanocapsule	Pacira Pharmaceuticals
Nanotax®	Paclitaxel	Solid tumors	Albumin-based nanocapsule	CritiTech Inc.
DaunoXom®	Daunorubicin	Kaposi's sarcoma	Liposomal nanocapsule	Galen Ltd.
Rapamune®	Sirolimus	Immunosuppressant	Polymeric nanocapsule	Pfizer Inc.
Visudyne®	Verteporfin	Age-related macular degeneration	Liposomal nanocapsule	Bausch & Lomb

DISCUSSION:

There are numerous chances to improve treatment efficacy while reducing side effects as a result of research into nanocapsules as cutting-edge drug delivery methods. These cutting-edge carriers offer a strong platform for reaching high drug encapsulation efficiency and regulated release profiles because of their distinctive core-shell architecture. Targeting particular tissues, including cancers, where targeted drug delivery can greatly enhance treatment outcomes while lowering systemic toxicity, is made easier with this structural design. Modulating the release kinetics of encapsulated medications enables long-lasting therapeutic benefits, which is essential for controlling long-term illnesses and maximizing pharmacotherapy.

The composition of nanocapsules, which can be made from both natural and synthetic polymers, further emphasizes their adaptability. This adaptability makes it possible to encapsulate a variety of therapeutic agents, including hydrophilic and hydrophobic chemicals, expanding their use in a range



of medical specialties, such as infectious illnesses, cardiology, and oncology. For example, using natural biodegradable polymers like alginate and chitosan improves biocompatibility and satisfies the growing need for eco-friendly medication delivery methods. On the other hand, synthetic polymers such as poly(lactic-co-glycolic acid) (PLGA) provide fine control over mechanical characteristics and rates of degradation, enabling customized drug release profiles that can be modified in accordance with particular therapeutic requirements.

Furthermore, improving the specificity of drug delivery requires the incorporation of functionalization techniques such the attachment of targeted ligands. Researchers can greatly lessen off-target effects and enhance patient outcomes by using ligands that bind preferentially to receptors that are overexpressed on target cells. In cancer therapy, when the objective is to maximize drug accumulation in tumor tissues while avoiding exposure to healthy cells, this focused strategy is very advantageous. Furthermore, the addition of stimuli-responsive components, including materials that are sensitive to temperature or pH, can improve the release mechanisms even further and enable on-demand drug administration in response to particular biological cues.

The creation of nanocapsules has become more scalable and reproducible due to advancements in manufacturing techniques such spray drying, coacervation, and liposome entrapment. These techniques guarantee that nanocapsules may be generated reliably and effectively on a wider scale, easing the move from lab research to clinical applications. Successful therapeutic interventions depend on predictable pharmacokinetics and biodistribution, which can only be achieved by producing nanocapsules with consistent size and shape.

The field of nanocapsule technology still faces a number of obstacles in spite of these encouraging advancements. Thorough safety analyses are crucial, especially when it comes to the possible toxicity of certain of the components utilized in nanocapsule formulations. Because of the special qualities of nanomaterials, new criteria and norms must be established for their review and approval, making regulatory compliance another major challenge. To overcome these obstacles and guarantee that nanocapsules may be safely and successfully incorporated into clinical practice, researchers, regulatory bodies, and industry stakeholders must work together.

Future studies should concentrate on improving the functioning and design of nanocapsules, investigating new materials that may improve their effectiveness, and creating intelligent delivery systems that react to certain biological cues. More effective and focused medication delivery systems may potentially be made possible by advancements in nanotechnology, such as the use of AI and machine learning in the design phase. Nanocapsules have great promise for transforming drug delivery and therapeutic approaches as the area of nanotechnology develops further, offering better



treatment options for a range of illnesses. Ultimately, a revolutionary change in contemporary medicine may result from the successful application of nanocapsule technology in clinical settings, which could produce more potent treatments, fewer adverse effects, and improved patient quality of life.

CONCLUSION:

A revolutionary development in drug delivery systems, nanocapsules provide a flexible and efficient platform for boosting therapeutic efficacy while reducing side effects. They are extremely well-suited for targeted therapeutics, notably in oncology, due to their distinctive core-shell architecture, which enables excellent drug encapsulation efficiency and regulated release profiles. The possibility for surface functionalization, stimuli-responsive release mechanisms, and the capacity to encapsulate a wide variety of therapeutic substances make nanocapsules a viable way to overcome the drawbacks of traditional drug delivery techniques.

The continuous advancement of nanocapsules, which employ both natural and synthetic polymers, highlights their versatility in a range of medical domains, such as infectious illnesses and cardiology. However, thorough safety assessments and adherence to legal requirements are necessary for the effective transition of nanocapsule technology from lab research to clinical applications. To overcome these obstacles and guarantee the secure introduction of nanocapsules into clinical practice, cooperation between researchers, regulatory agencies, and industry participants will be crucial.

Future studies should focus on improving the functionality and design of nanocapsules, investigating new materials and creative production methods to improve their performance. The creation of intelligent delivery systems that can react to certain biological cues may be further enhanced by the integration of cutting-edge technology like artificial intelligence and machine learning. Nanocapsules have a significant potential to transform drug delivery and therapeutic approaches as nanotechnology develops further, offering better treatment options and better patient outcomes. A major breakthrough in contemporary medicine could result from the successful application of nanocapsule technology in clinical settings, which could ultimately lead to more potent treatments, fewer adverse effects, and an overall improvement in patients' quality of life.

REFERENCES:

1. Singh R, Lillard Jr JW. Nanoparticle-based targeted drug delivery. *Experimental and molecular pathology*. 2009 Jun 1;86(3):215-23.
 2. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano letters*. 2010 Sep 8;10(9):3223-30.
- Cuest.fisioter.2025.54(4):5093-5117



3. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. *Journal of controlled release*. 2001 Jan 29;70(1-2):1-20.
4. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids and surfaces B: biointerfaces*. 2010 Jan 1;75(1):1-8.
5. Wang X, Jiang Y, Wang YW, Huang MT, Ho CT, Huang Q. Enhancing anti-inflammation activity of curcumin through O/W nanoemulsions. *Food chemistry*. 2008 May 15;108(2):419-24.
6. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. *Nature reviews Drug discovery*. 2014 Nov;13(11):813-27.
7. Müller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Advanced drug delivery reviews*. 2002 Nov 1;54:S131-55.
8. Brannon-Peppas L, Blanchette JO. Nanoparticle and targeted systems for cancer therapy. *Advanced drug delivery reviews*. 2004 Sep 22;56(11):1649-59.
9. Almeida AJ, Souto E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advanced drug delivery reviews*. 2007 Jul 10;59(6):478-90.
10. Ma Z, Yeoh HH, Lim LY. Formulation pH modulates the interaction of insulin with chitosan nanoparticles. *Journal of pharmaceutical sciences*. 2002 Jun 1;91(6):1396-404.
11. Danhier F, Ansorena E, Silva JM, Coco R, Le Breton A, Préat V. PLGA-based nanoparticles: an overview of biomedical applications. *Journal of controlled release*. 2012 Jul 20;161(2):505-22.
12. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro-and nanoparticles in drug delivery. *Journal of controlled release*. 2004 Nov 5;100(1):5-28.
13. Koo H, Huh MS, Sun IC, Yuk SH, Choi K, Kim K, Kwon IC. In vivo targeted delivery of nanoparticles for theranosis. *Accounts of chemical research*. 2011 Oct 18;44(10):1018-28.
14. Koo H, Huh MS, Sun IC, Yuk SH, Choi K, Kim K, Kwon IC. In vivo targeted delivery of nanoparticles for theranosis. *Accounts of chemical research*. 2011 Oct 18;44(10):1018-28.
15. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. *Journal of controlled release*. 2001 Jan 29;70(1-2):1-20.
16. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids and surfaces B: biointerfaces*. 2010 Jan 1;75(1):1-8.
17. Singh R, Lillard Jr JW. Nanoparticle-based targeted drug delivery. *Experimental and molecular pathology*. 2009 Jun 1;86(3):215-23.
18. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano letters*. 2010 Sep 8;10(9):3223-30.



19. Brannon-Peppas L, Blanchette JO. Nanoparticle and targeted systems for cancer therapy. *Advanced drug delivery reviews*. 2004 Sep 22;56(11):1649-59.
20. Almeida AJ, Souto E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advanced drug delivery reviews*. 2007 Jul 10;59(6):478-90.
21. Szejtli J. Past, present and future of cyclodextrin research. *Pure and Applied Chemistry*. 2004 Jan 1;76(10):1825-45.
22. McClements DJ. Encapsulation, protection, and delivery of bioactive proteins and peptides using nanoparticle and microparticle systems: A review. *Advances in colloid and interface science*. 2018 Mar 1;253:1-22.
23. Anandharamakrishnan C. Spray drying techniques for food ingredient encapsulation. John Wiley & Sons; 2015 Jul 23.
24. Wang JX, Guo W, Xiong K, Wang SN. Review of aerospace-oriented spray cooling technology. *Progress in Aerospace Sciences*. 2020 Jul 1;116:100635.
25. Bakry AM, Abbas S, Ali B, Majeed H, Abouelwafa MY, Mousa A, Liang L. Microencapsulation of oils: A comprehensive review of benefits, techniques, and applications. *Comprehensive reviews in food science and food safety*. 2016 Jan;15(1):143-82.
26. Jafari SM, Assadpoor E, He Y, Bhandari B. Encapsulation efficiency of food flavours and oils during spray drying. *Drying technology*. 2008 Jul 1;26(7):816-35.
27. Mehandole A, Walke N, Mahajan S, Aalhat M, Maji I, Gupta U, Mehra NK, Singh PK. Core-shell type lipidic and polymeric nanocapsules: the transformative multifaceted delivery systems. *AAPS PharmSciTech*. 2023 Jan 26;24(1):50.
28. Deeksha S, Deeksha J, Pragati N, Siddhesh B, Palekar S, Risbud G. Safety Assessment of Consumption of Proso Millet and Milk (A case study with Ayurveda perspective). *MILLETS—2023: A Transdisciplinary Approach to its Resurgence and Sustainability*. 2023 Oct 6:246.
29. Prasad N, Meyyappan J, Dhanorkar M, Kushwaha R, Mandal K, Veeranki V, Behera M, Patel M, Yadav B, Bhadauria D, Kaul A. Novel mutation patterns in children with steroid-resistant nephrotic syndrome. *Clinical Kidney Journal*. 2024 Aug;17(8):sf218.
30. Carson L, Merkatz R, Martinelli E, Boyd P, Variano B, Sallent T, Malcolm RK. The vaginal microbiota, bacterial biofilms and polymeric drug-releasing vaginal rings. *Pharmaceutics*. 2021 May 19;13(5):751.
31. Erdoğan N, Akkın S, Bilensoy E. Nanocapsules for drug delivery: an updated review of the last decade. *Recent patents on drug delivery & formulation*. 2018 Dec 1;12(4):252-66.



32. Shaji J, Patole V. Protein and peptide drug delivery: oral approaches. *Indian journal of pharmaceutical sciences*. 2008 May;70(3):269.
33. Bozzuto G, Molinari A. Liposomes as nanomedical devices. *International journal of nanomedicine*. 2015 Feb 2;975-99.
34. Mozafari MR, Khosravi-Darani K, Borazan GG, Cui J, Pardakhty A, Yurdugul S. Encapsulation of food ingredients using nanoliposome technology. *International Journal of Food Properties*. 2008 Nov 18;11(4):833-44.
35. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. *Advanced drug delivery reviews*. 2013 Jan 1;65(1):36-48.
36. Abdul-Al M, Saeinasab M, Sefat F. Encapsulation techniques overview. In *Principles of Biomaterials Encapsulation: Volume One* 2023 Jan 1 (pp. 13-36). Woodhead Publishing.
37. Dube A, Nicolazzo JA, Larson I. Chitosan nanoparticles enhance the intestinal absorption of the green tea catechins (+)-catechin and (–)-epigallocatechin gallate. *European Journal of Pharmaceutical Sciences*. 2010 Oct 9;41(2):219-25.
38. Wang X, Xu B, Chen Z, Del Col D, Li D, Zhang L, Mou X, Liu Q, Yang Y, Cao Q. Review of droplet dynamics and dropwise condensation enhancement: Theory, experiments and applications. *Advances in Colloid and Interface Science*. 2022 Jul 1;305:102684.
39. Zhang L, Gu FX, Chan JM, Wang AZ, Langer RS, Farokhzad OC. Nanoparticles in medicine: therapeutic applications and developments. *Clinical pharmacology & therapeutics*. 2008 May;83(5):761-9.
40. Zoabi A, Touitou E, Margulis K. Recent advances in nanomaterials for dermal and transdermal applications. *Colloids and Interfaces*. 2021 Mar 18;5(1):18.
41. Li Y, Zhang R, Zhang Q, Luo M, Lu F, He Z, Jiang Q, Zhang T. Dual strategy for improving the oral bioavailability of resveratrol: Enhancing water solubility and inhibiting glucuronidation. *Journal of Agricultural and Food Chemistry*. 2021 Aug 6;69(32):9249-58.
42. Fang Z, Bhandari B. Encapsulation of polyphenols—a review. *Trends in food science & technology*. 2010 Oct 1;21(10):510-23.
43. Khezerlou A, Tavassoli M, Alizadeh Sani M, Mohammadi K, Ehsani A, McClements DJ. Application of nanotechnology to improve the performance of biodegradable biopolymer-based packaging materials. *Polymers*. 2021 Dec 15;13(24):4399.
44. Tan C, Xie J, Zhang X, Cai J, Xia S. Polysaccharide-based nanoparticles by chitosan and gum arabic polyelectrolyte complexation as carriers for curcumin. *Food Hydrocolloids*. 2016 Jun 1;57:236-45.



45. Yan J, Mangolini F. Engineering encapsulated ionic liquids for next-generation applications. *RSC advances*. 2021;11(57):36273-88.
46. Bhutkar SP, Millard PE, Preece JA, Zhang Z. Microplastic-free microcapsules using supramolecular self-assembly of bis-urea molecules at an emulsion interface. *Langmuir*. 2024 Jul 11;40(29):14798-810.
47. George M, Abraham TE. Polyionic hydrocolloids for the intestinal delivery of protein drugs: alginate and chitosan—a review. *Journal of controlled release*. 2006 Aug 10;114(1):1-4.
48. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers*. 2011 Aug 26;3(3):1377-97.
49. Kaniuk Ł, Stachewicz U. Development and advantages of biodegradable PHA polymers based on electrospun PHBV fibers for tissue engineering and other biomedical applications. *ACS biomaterials science & engineering*. 2021 Oct 15;7(12):5339-62.