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REVIEW ON PREPARATION TECHNIQUES AND CHARACTERIZATION OF NANOCAPSULES

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ABSTRACT:

Nano capsules are a new type of nanomaterials that are widely used in various fields of science and technology. They are made up of a variety of materials, including polymers, surfactants, and polymers. In this review, we will focus on the recent developments in the field of nanocapsule formulation, focusing on the application of nanocapsules in drug delivery and delivery. We will also review the recent advancements in the fields of drug delivery, nanoencapsulation, nanorobotic systems, and nanorobotics. The List of FDA-approved nanotechnology-based products and the clinical trials is also included in this review article.

Keywords: Nanocapsules, polymers, drug delivery system, emulsion, biodegradable.

1. INTRODUCTION:

Nanotechnology is the study of particles that are either a particulate dispersion or solid particles, and range in size from 0.1-100 nm. Nanoparticles include both nanospheres and nanocapsules. Undefined The choice of preparation method defines that we get nanoparticles, nanospheres, or nanocapsules. Nanocapsules consist of a protective shell and one or more active materials (core) that contain the therapeutic substance[1]. These spherical, hollow nanoparticles can filled with a polar or nonpolar solvent and a desired substance. In contrast

to nanocapsules, nanospheres are matrix systems in which the drug is uniformly spread and enclosed by a special polymer membrane. From a pharmaceutical perspective, nanocapsules are particularly attractive due their oil-based central cavities, which enable enhanced medication administration by allowing a high level of lipophilic material encapsulation[2].
Nano-drug delivery systems have become increasingly popular due to their ability to improve drug efficacy and reduce toxicity. One such system is the nanocapsule, which is a submicron-sized particle with a polymeric wall and an oil core that can be designed using interfacial nano-deposition or interfacial polymerization technologies[3]. Nanocapsules have few advantages, including sustained drug release, increased bioavailability,and targeted drug delivery. They are particularly useful for protecting enzymes, proteins, and foreign cells, and can be used for the controlled release of pharmaceuticals[4]. However, the inert carrier materials used in nanocapsules having the low drug-loading capacities, requiring the use of excessive parenteral excipients. Despite this, nanocapsules remain a promising drug delivery system in the biomedical field[5]
Nanocapsules are a type of nanoparticle that stands out due to their distinct core-shell structure. Particularly, when polymers are used in their fabrication, they are referred to as hollow polymer nanostructures. Encapsulation technologies have been available for a long time, with a focus on the controlled release of nutraceuticals, oxidation removal, and mitigation of hygroscopic and chemical interactions[6].

POLYMERIC MATERIALS FOR PREPARING NANOCAPSULES:
Nano-capsules are prepared using two types of polymers: there is the natural polymers and synthetic polymers.

1. Natural
polymers, such as proteins, enzymes, muscle fibres, polysaccharides, and gummy exudates, have been successfully used in formulating various medicinal products. In the pharmaceutical industry, natural polymers chitosan, carrageenan, ispaghula, acacia gum, agar-agar, gelatin from animals or plants such as seaweed (vegetarian option), guar gum derived from legumes like beans and lentils , shellac resin secreted by the lac beetle insect , and gum karay are commonly used as adjuvants, emulsifiers, and packaging adhesives. Alginate, a natural polysaccharide obtained from brown seaweed, is also widely used[4]. Gelatin, which is commonly found in food and pharmaceutical products, has a considerable impact on its mechanical characteristics, swelling behaviour, and thermal properties based on its cross-linking degree. Polyester made of poly (hydroxybutyrate-co-hydroxy valerate) PHBV is manufactured by various microorganisms and also utilized[7]

2. Synthetic Polymer:
Synthetic polymers are mostly Man-made polymers, categorized into four primary groups based on their utility: thermoplastics, thermosets, elastomers, and synthetic fibres. They are widely used in consumer goods such as money, superglue, etc. There are numerous synthetic polymers available with different main chains and side chains[4].
Among them, several synthetic polymeric materials containing polyhydroxy acids, Polymers that have been used are poly (lactic acid) (PLA), poly (lactic-co-glycolic acid) (PLGA), cross-linked polyesters such a poly-caprolactone (PCL), poly (alkyl cyanoacrylate) (PACA), and Eudragit series which include Eudragit S100, Eudragit E, Eudragit RS.
PLA is a biocompatible and biodegradable polymeric ester in which the physical breakdown products in the body mirror lactic acid, a monomer and an intermediate of carbohydrate catabolism. Among all the biodegradable polymers, PLGA copolymers have been widely

employed for nanocapsule formulation due to factors related to degradation and mechanical characteristics of the polymer. PACA is environmentally friendly; non-toxic, non-inflammatory, non-immunogenic and non-carcinogenic natural polymer, which has attracted enormous interest for the controlled and site specific drug delivery.

Eudragit types are copolymers of methacrylic acid and methacrylate and `since the ratios of the materials are different, there are many types of it. paper is often used in substance coatings of drugs and other pharmaceutical products. They pointed at such advantages of synthetic polymers as higher purity and much better possibility of reproaching in comparison with polymers gained through natural means. Due to their bio-compatibility and bio-degradation to harmless metabolites they have received a lot of interest. [8][9][10].

TECHNIQUES OF PREPARATION:

- Nano-capsules prepared by various methods like [4][1][7][5][11].
- Solvent Evaporation
- Nano Precipitation
- Emulsion diffusion method
- Double emulsification method
- Emulsion coacervation method
- Layer-by-layer assembly method

1. Solvent Evaporation

The earliest technique developed for creating nanoparticles is solvent evaporation. In this technique, polymer solutions which are prepared in the volatile solvents and emulsions are created using dichloromethane or chloroform[12]. However, ethyl acetate is now employed in place of these solvents because it is safer to use when compared to the latter. Preparation here refers to the process of formation of the nanoparticles in which, the solvent is eliminated thereby changing the paste-like emulsion to a suspension. In this case, this solution is then permitted to diffuse through the continuous phase of the emulsion with the help of other ordinary methods such as single or double emulsion.[13]. In preparation of the nanoparticles, high-speed homogenization or ultrasonication are applied and the solvent is then removed either by magnetic stirring at room temperature for a time or under reduced pressure. This leads to the precipitation of nanosized particles in a fully solidified state, then after the particles have been ultra-centrifuged, washed to remove any associated surfactants and finally freeze-dried. [14][15].

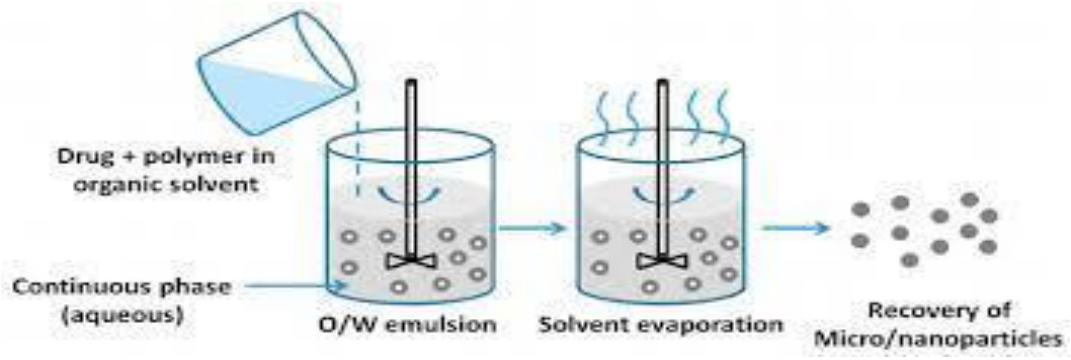
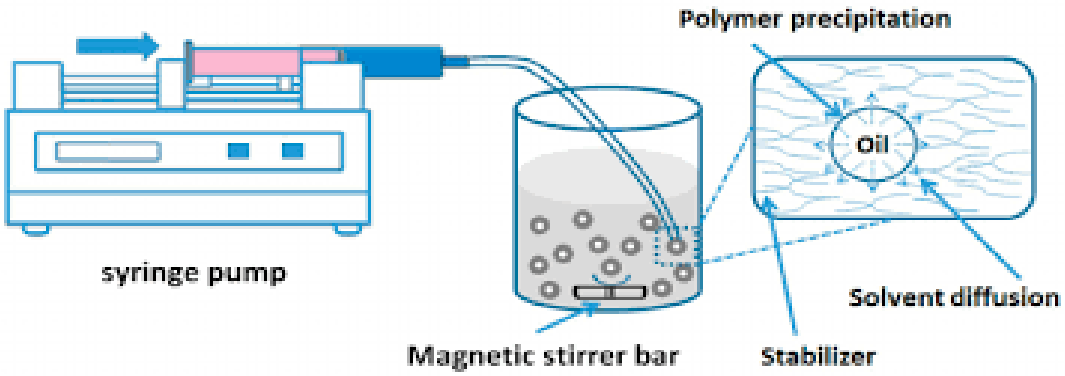


Fig.1. Solvent Evaporation Method [16]

The nanoprecipitation method is a widely used technique for creating polymeric nanoparticles[17]. This method is economical on energy, gentle and does not demand much

force. In this approach, polymers of the organic solutions which may include acetone, ethanol, or methanol are incorporated in the preparation process after which the diffusion of the organic solvent takes place. [18].The process typically utilizes the intermediate polarity PLA polymer, which is allowed to dissolve in a water-miscible solvent, leading to the formation of nanospheres (19)(20). The solution is then added to an aqueous solution containing a stabilizer as a surfactant, where it interacts with the organic solvent to form nanoparticles(21). An interesting outcome of this method is the "Ouzo" effect, which refers to the scattering of



nanoparticles caused by nano-precipitation in non-solvent solutions without the use of surfactants or hydrophobic substances(4).

Fig.2. Nanoprecipitation method(16)

2. Emulsion diffusion method

The Emulsification or Solvent Diffusion (ESD) technique is a modified version of the solvent evaporation method. It uses a water-miscible solvent and a small amount of water-miscible organic solvent to generate turbulence between the two phases(7). This technique results in the formation of Nanosized particles that can encapsulate both lipophilic and hydrophilic active substances(22). The oil phase in this technique uses a water-miscible organic solvent, along with a minor amount of the water-miscible organic solvent. The commonly used biodegradable polymers in this technique are PCL, PLA, and eudragit, while poly (hydroxybutyrate-co-hydroxy valerate) (PHBHV) may also be used(23).

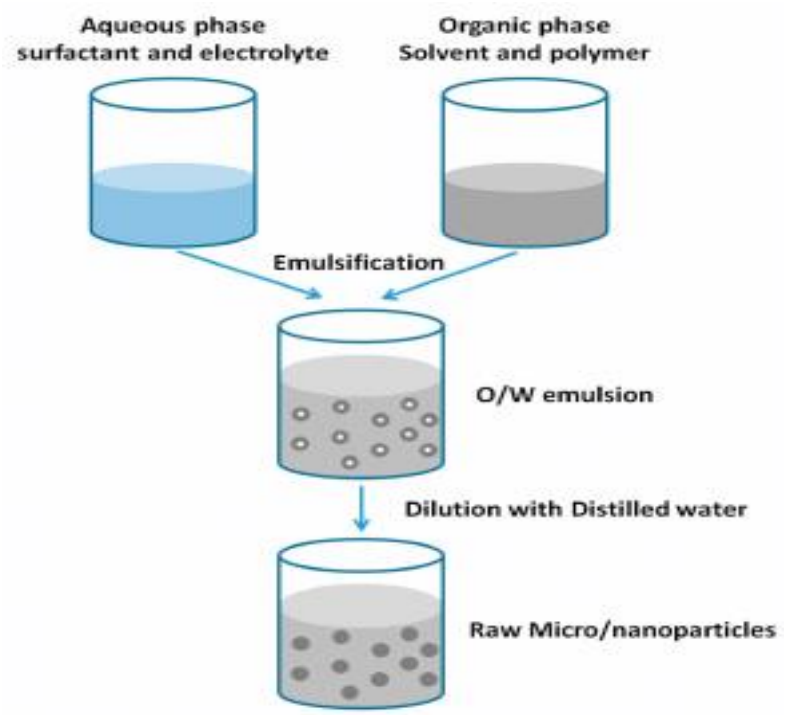


Fig.3. Emulsion diffusion method(16)

3. Double Emulsification Method

Double emulsions are advanced formations that involve at least two emulsions systems which in this case are O/W/O and W/O/W. Depending on the type of media that is used, the emulsions can be of two types – the water-oil-water type (w/o/w) and the oil-water-oil type (o/w/o) (24). In the nanoencapsulation process, core material is initially dispersed into the wall-material containing solution and the formed mixture again dispersed into the medium in the droplet form. Last but not the least, to get the desired nanoencapsulation, the medium in the continuous phase is eliminated. Thus, w/o emulsions are the most suitable for water soluble drug nano encapsulation and the preparative nanocapsules exhibited high drug entrapment efficiency and high drug carrying capacity, with longer half-life(25).

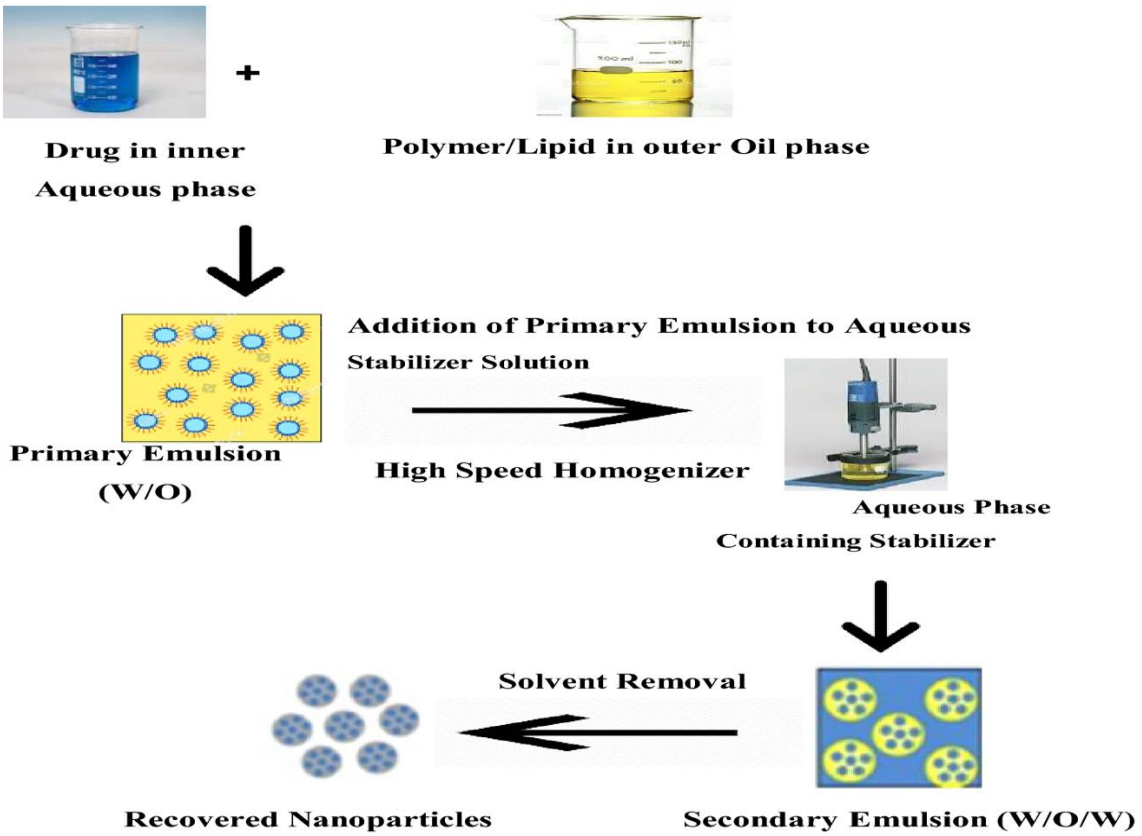


Fig.4. Double emulsification method(26)

4. Emulsion Coacervation method

Emulsion-coacervation is the process of preparing an emulsion of organic phase, which comprises oil, active substance, and solvent and an aqueous phase, which contains water, polymer, and stabilizing agent by mechanical stirring or ultrasonication. This is succeeded by cross-linking that stiffens the structure of the nanocapsule shell(27)(28). The method involves chitosan polymer, di-block co-polymer of either ethylene oxide or propylene oxide (PEO-PPO) and a polyanion (sodium tripolyphosphate) to form coacervation products which are particles of sizes in the nanometer range. Such coacervates are made up of chitosan's positively charged amino group that can react with the negatively charged tri polyphosphate thus presenting a stable drug delivery system (28)..

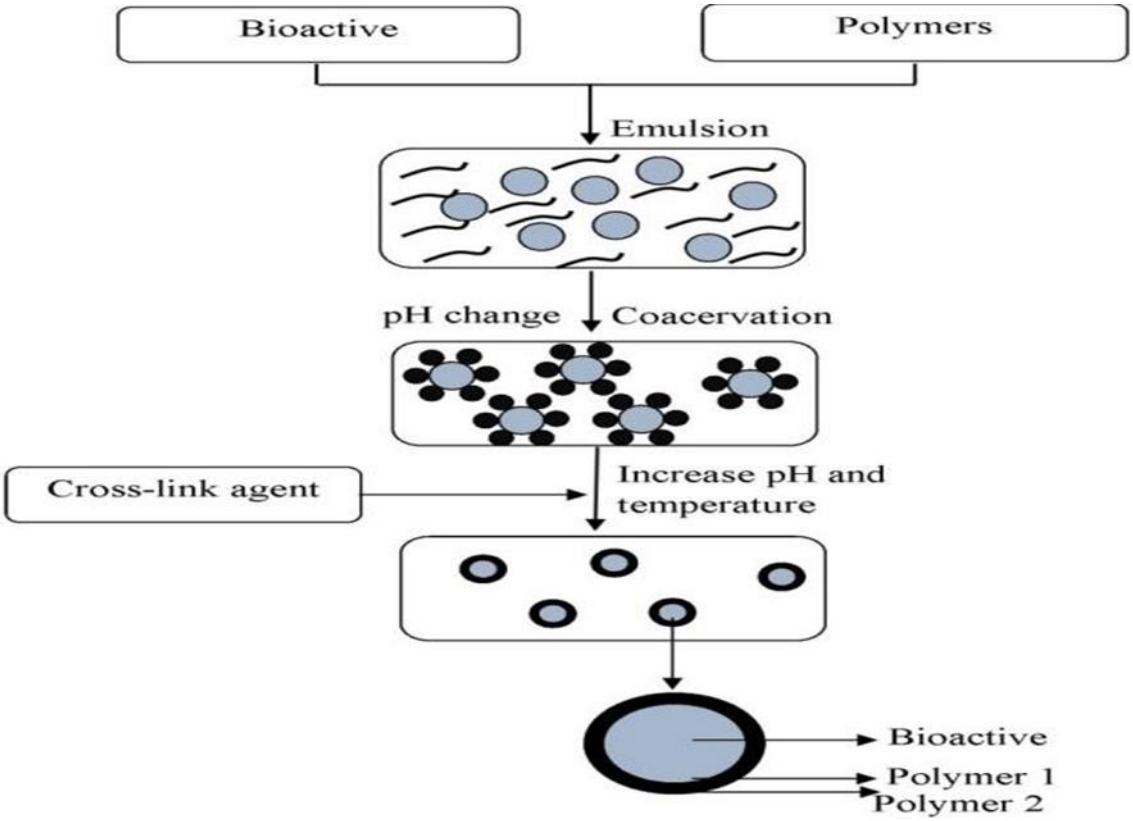


Fig.5. Emulsion Coacervation method(29)

5. Layer Layer Assembly method.

The Layer-by-Layer (LBL) technique is a modern method for depositing thin films, especially those with opposite charges (30). This process can also be used to create nano-capsules. In this technique, colloidal particles act as templates and adsorb a polymer layer in a polymer solution. The polymer layers are then progressively deposited one after the other by repeating the technique with a second polymer(31)(32). Some polycations used in the LBL method are polylysine, chitosan, gelatin B, poly (allylamine) (PAA), poly (ethyleneimine) (PEI), amino dextran, and protamine sulphate. The polyanions that have been employed are; poly (styrene sulfonate) (PSS), sodium alginate, poly (acrylic acid), dextran sulfate, carboxymethyl cellulose, hyaluronic acid, gelatin A, chondroitin and heparin. These nanocapsules are very useful for bio-separation and site specific delivery of drugs(33)..

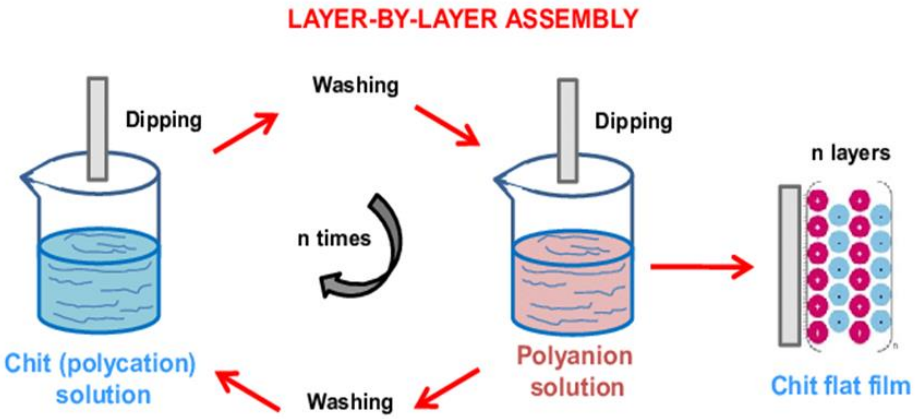


Fig.6. Layer By Layer Assembly Method(34)

CHARACTERIZATION OF NANOCAPSULES:

- Particle size
- Surface characteristics and zeta potential
- Fluorescence quenching
- Encapsulation Efficiency
- Active Substance Release
- Stability

1. Particle size

Particle size and size distribution of nanocapsules in a system are very important factors that influence biodistribution, bioavailability, biotoxicity and targeting property. Also, they significantly influence the stability of nanoparticulate systems and loading and release of a drug. Particle size also influences the released dose and the time of pharmacological action since smaller particle size means larger surface area, and the drug released quickly, while large particle size has large core surface and diffused out slowly. Particle size also plays a role in degradation of a polymer(35). Methods like laser light diffraction (LLD), dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), fluorescence correlation spectroscopy (FCS) are widely known to calculate diffusion coefficient, size and mass of nanoparticles (36). , field-flow fractionation (FFF), quadrupole magnetic field-flow fractionation (Mg FFF) is an analytical separation and characterization of nano- and micro-sized particles(37). Mg FFF has also been used in the later characterization of magnetic nanoparticles(38). CE technique has been shown to be applicable to the separation of nanometre-scale particles(39). The particle size analysis of the formulations was done using Malvern Master sizer MS, and mean particle size and particle size distribution of each nano capsular dispersion was noted.(8).

2. Surface Characteristics and Zeta Potential

Zeta potential and hydrophobic/hydrophilic degree are the most extensively studied surface characteristics of nanocapsules. The chemical nature of the polymer, the chemical composition of the stabilising agent and the pH of the medium are the key factors that influence the zeta potential of nanocapsules (40). "The value can be ascertained through the utilization of Zeta Plus(41), or PCS, and laser Doppler anemometry(42), which will have an impact on the dispersion stability of nanocapsules. The hydrophobicity of nanocapsule surfaces can be evaluated using hydrophobic interaction chromatography(43). One effective way to target drugs using nanocapsules is to apply a surface coating of nanocapsules that contains hydrophilic polymers and/or hydrophilic surfactants. Additionally, the use of biodegradable copolymers of hydrophilic segments like polyethene glycol (PEG), polyethene oxide (PEO), polyoxamer, polyxamine, and polysorbate 80 in the formulation of the nano capsules has proven successful. The zeta potential of the nanocapsule is an efficient method to characterize the charge on its surface(44)(45).

3. Fluorescence quenching

Quenching of fluorescence(46) is mainly utilized to confirm the localization of nanocapsules, which contain the aqueous core containing oligonucleotides(47)

4. Encapsulation Efficiency

To enhance drug delivery and reduce the frequency of administration, it is advantageous to develop a nanoparticulate system with high drug encapsulation efficiency. However, the conventional double emulsion approach is challenging, time-consuming, and has poor drug encapsulation effectiveness. To improve the efficacy of drug encapsulation for W/O/W

emulsion, researchers have made significant efforts and controls. Encapsulation of drugs in nanocapsules, such as Xerogels and Aerosol 200, can delay the release of drugs, making them ideal for use as encapsulated materials(5). Entrapment efficiency was calculated according to the following equation(11).

Entrapment efficiency= The total amount of entrapped drug in nanocapsule/
The total amount of drug included in preparation X 100

5. Active Substance Release

To determine the amount of free drug in formulations, a solvent that dissolves only the free drug and not the other ingredients was used. The free drug was determined in the supernatant, and the filtrate was made up to volume with 0.1 N HCl and filtered through a Whatman filter (size 44) to evaluate the presence of free drugs. In vitro, release tests were performed under the required pH (phosphate buffers) and 37°C to calculate the cumulative per cent release of the drug over time(48). Active ingredient release characteristics can be tested using dissolution experiments, while dispersion stability characteristics can be tested by measuring changes in the zeta potential and particle size of the nanocapsules (7).

6. Stability

Accelerated stability testing is a crucial process to evaluate the stability of medication formulations in extreme environmental conditions such as temperature, humidity, and light exposure. These studies are performed at varying temperatures ranging from below zero to 60°C, including standard room temperature and 37°C and 50°C. The short-term stability of the formulation can be assessed by conducting tests for two months. For nano-capsule formulations, the samples should be stored between 4°C and 25°C for 60 days. During this time, it is recommended to remove five millilitres of the sample every week to check the drug content and observe any physical changes that may occur throughout the storage period(11)(49).

- **EVALUATION:**

1. **X-ray diffraction studies (XRD)**

Differential Scanning Calorimetry (DSC) is an advanced analytical technique that is capable of identifying and measuring a wide range of physical properties and thermal transitions in polymeric materials. By accurately estimating the entropy and enthalpy values associated with melting and mesomorphic transitions, DSC can provide invaluable insights and data to researchers and industry professionals in the field. As such, it is an indispensable tool for anyone seeking a comprehensive understanding of polymeric materials and their properties(50)(5)

2. **Scanning Electron Microscopy (SEM)**

Scanning Electron Microscopy (SEM) is a high-resolution imaging technique that helps in analyzing the morphology and composition of nanoparticles. It uses a low-energy beam of electrons to scan the surface of the sample, providing image resolutions in the low nanometre range. The complex architecture of hierarchical branching aggregates, such as nanocapsules, can be characterized by observing their flocculent structures, small and big clusters, and big branches, all of which can be visualized at different scales using SEM(4).

3. **Differential Scanning Calorimetry (DSC)**

Differential Scanning Calorimetry (DSC) is a highly effective analytical technique utilized to identify and quantify various physical properties and thermal transitions of polymeric

materials. It provides valuable insights into the melting and mesomorphic transitions and their associated entropy and enthalpy
values, making it an invaluable tool for researchers and industry professionals who require accurate and detailed information about polymeric materials (4)(5).

4. **Transmission Electron Microscopy (TEM)**

TEM is a method for visualizing the internal structure of solids by transmitting a beam of high-energy electrons through the material. This technique is utilized to examine small specimens and observe their features. The technology involves accelerating a beam of electrons, which passes through an incredibly thin sample, allowing scientists to observe details such as structure and morphology(4) (5)

5. **X-Ray Photoelectron Spectroscopy (XPS)**

X-ray photoelectron spectroscopy (XPS) is a quantitative analytical technique that enables the measurement of the elemental composition of a material's surface, while simultaneously determining the binding states of the constituent elements. It is also referred to as electron spectroscopy for chemical analysis (ESCA) and is an indispensable tool for the investigation of a material's surface chemistry. XPS is capable of providing insights into the elemental composition, chemical state, and electronic properties of the atoms situated at or near the surface of a material.

6. **Multi-angle laser Light Scattering (MALLS)**

Is a technique that has been widely used for the study of vault particles, which consist of a thin shell enveloping a large internal volume. These particles have tremendous potential for applications in compound distribution, encapsulation, and protection. By examining the conformation of the vault particles in solution using MALLS, one can investigate the interconversion of the opened and closed conformers. Such studies are crucial for the control of the entrapment and release of encapsulated components in nanocapsule applications. Additionally, vaults with toxic metal binding sites are of great significance in both environmental and medical detoxification (4).

7. **FT-IR Analysis**

FTIR spectroscopy is a powerful analytical technique used to identify organic, polymeric, and, in some cases, inorganic materials. It works by using infrared radiation to scan test samples and observe their chemical properties. By analyzing the resulting spectra, we can confirm the presence of characteristic peaks that correspond to the functional groups present in the sample. These peaks provide valuable information about the sample's chemical composition and structure, making FTIR a widely used technique in a variety of fields, from materials science to pharmaceuticals (4)(5).

APPLICATION:

- Drug Delivery System Carriers
- Treatment of Cancer
- Nutraceuticals
- Self-Healing Material
- Therapeutic and Diagnostic Applications
- Food Science and Agriculture
- Cosmetics

1. Drug Delivery System Carriers

Polymeric nanocapsules have emerged as a promising drug delivery system due to their unique characteristics, including the potential for targeted drug delivery. These nanocapsules can specifically target tumour tissues by taking advantage of the increased microvascular permeability in these tissues, which enhances their penetration and retention. As a result, the nanocapsules can accumulate in tumour tissues and deliver tumour-targeted drugs through tumour-specific lymph excretion. Recent studies have demonstrated that polymeric nanocapsules are more efficient than liposomes and emulsions as lymphatic targeting drug carriers, making them a promising new approach for cancer treatment (7). Polymer shells that are soluble in water are being developed to transport a protein known as apoptin into malignant cells. These shells have a size of 100 nm (11). Polymeric nanocapsules have great potential in the field of Controlled or Sustained-release Drug Delivery due to their ability to localize the drug at the sites of action and enhance skin penetration of active ingredients. The rate of degradation of polymers is a critical factor that determines the release rate of the encapsulated drug, which is influenced by the crystallinity, hydrophobicity, and molecular weight of the polymers. Low degradation rate polymers like PLGA are ideal for preparing sustained-release nanocapsules. Researchers have conducted extensive studies on polymeric nanocapsules as drug delivery carriers to improve transdermal and dermal delivery of biologically active components. This is attributed to their extremely small particle size and hydrophilic and hydrophobic surface properties (7).

2. Treatment of Cancer

The use of nanoparticles for targeting tumours is based on the ability of nanoparticles to deliver a high concentration of drugs to the tumour site through either the enhanced permeability and retention effect or active targeting. Additionally, nanoparticles can limit the distribution of drugs to healthy tissues, reducing their exposure (51). Astatine, a radioactive compound, emits high-velocity alpha particles through the process of radioactive decay. These alpha particles are about 4,000 times faster than the beta decay of emitted electrons. Due to their unique characteristics, including low penetrating power and large particle size, alpha particles are commonly used for cancer treatment. Their ability to target tumours at the single cellular level makes them highly effective (5). Polymer shells that dissolve in water are being developed to transport apoptin, a protein, into cancerous cells. The size of these capsules is 100 nm (11).

3. Nutraceuticals

Nutraceuticals refer to bioactive compounds that are added to food to provide health benefits beyond basic nutrition. These compounds are often encapsulated in nanocarriers, which serve as delivery vehicles to enhance their bioavailability. The effectiveness of these carriers is dependent on their size, with smaller carriers generally showing greater efficacy (11).

4. Self-Healing Material

The incorporation of nanocapsules into materials such as microelectronics parts, polymeric coatings, and adhesives can significantly reduce high-load damage. These nanocapsules disperse throughout the polymer and enhance the healing process of cracks within the materials. Dicyclopentadiene (DCPD) is a commonly used material that is produced on-site within the material through a process known as sonication (52). Polymer coatings, adhesive parts, microelectronics, and structural composites can suffer from damages that may last for extended periods. To address this issue, a self-healing technique has been developed using polymer microcapsules that contain a healing agent. This technique provides adequate strength and has a long shelf life, while also binding well to the host material. The development of nanocapsules with functionalized surfaces and walls capable of forming nanometer-sized

objects has become popular. These advancements may lead to the creation of completely novel therapeutic applications in the fields of technology and medicine (53)

5. Therapeutic and Diagnostic Application

Magnetic Resonance Imaging (MRI) technology is being used to direct nanorobotic systems in a controlled manner for treating the human body at the cellular and subcellular levels. By generating better monitoring driving forces, an MRI scanner serves as the basis for an MRI-guided nanorobotic system that causes magnetic nanocapsules to explode at a specific target. Advanced engineering control algorithms and computational tools have been developed to administer nanocapsules in real time, following the driving force (54). - Magnetic Resonance Imaging (MRI), X-ray imaging, Fluorescence Imaging, Ultrasound Imaging, and Multi-Modal Bio imaging are some of the diagnostic applications where it is used (55).

6. Food Science and Agriculture

The process of nanoencapsulation in foods refers to the alteration of texture, flavour, colour, and shelf-life stability through the use of nanotechnology. This technique involves the encapsulation of food ingredients within nano-sized particles, which can offer several benefits such as improved solubility, controlled release, enhanced bioavailability, and increased stability. Furthermore, nanoencapsulation has the potential to protect bioactive compounds from degradation, improve sensory attributes, and enhance the functionality of food ingredients (56).

7. Cosmetics

This text describes a UV-blocking cosmetic product that uses TiO nanocapsules to increase stability and UV protection without causing harm to the body. The nanocapsules are made by dispersing TiO2 with two surfactants and using a surface treating agent containing isosteric acid or aluminium stearate to carry out an oleophilic surface procedure. Compared to standard solutions, the nanocapsules containing hinokitiol (HKL) and formed by the emulsion diffusion method exhibit growth stimulation and offer promising results with structural and histological changes of the hair follicles(5).

The List of FDA-approved nanotechnology-based products and clinical trials(57)**.**
Polymer nanoparticles-synthetic polymer particles combined with drugs or biologics

Name	Material Description	Nanoparticle Advantage	Indications	Approved year
Adagen ® (Sigma-Tau-Pharmaceuticals)	PEGylated adenosine deaminase enzyme	Improve circulation time and decrease immunogenicity	Severe combined Immunodeficiency Disease	1990
AmBisome ® (Gilead Sciences)	Liposomal Amphotericin B	Reduced Nephrotoxicity	Fungal/Protozoal Infections	1997
Abraxane®/ABI-007 (Celgene)	Albumin-bound paclitaxel nanoparticles	Improved solubility; improved	Breast Cancer, NSCLC, Pancreatic Cancer	2005

		delivery to tumour		
Copaxone ®/Glatopa (Teva)	The random copolymer of l-glutamate, l-alanine, l-lysine and l-tyrosine	Large amino-acid-based polymer with controlled molecular weight and clearance characteristics.	Multiple sclerosis (MS)	1996
Cimzia®/certolizumab pegol (UCB)	PEGylated antibody fragment (Certoli- Zumba)	Improved circulation time and greater stability) in vivo	Crohn's disease; Rheumatoid arthritis; Psoriatic Arthritis; Ankylosing Spondylitis	2008
DaunoXome® (Galen)	Liposomal daunorubicin	Increased delivery to tumour site; lower systemic toxicity arising from side effects	Karposi's Sarcoma	1995
DepoDur® (Pacira Pharmaceuticals	Liposomal morphine sulphate	Extended Release	Analgesia (post-operative)	2004
Doxil /Caelyx (Janssen)	Liposomal doxorubicin	Improved delivery to the site of disease; decrease in systemic toxicity of a free drug	Ovarian Cancer	2005
Focalin XR (Novartis)	Dexmethylphenidate HCl	Increased drug loading and bioavailability	Psychostimulant	2005
Feraheme™/ferumoxytol (AMAG pharmaceuticals)	Ferumoxytol SPION with poly			

glucose sorbitol carboxymethyl ether Magnetite suspension allows for prolonged steady release, decreasing the number of doses. Deficiency anaemia iron deficiency in Chronic Kidney disease. 2009 Ferrlecit (Sanofi Avertis) Sodium ferric gluconate Allows increased dose Iron deficiency in chronic kidney disease 1999 GastroMARK; umpire (AMAG pharmaceuticals) SPION coated with silicone Superparamagnetic character Imaging agent 2001 Krystex9xa® /pegloticase (Horizon)	Polymer-protein conjugate (PEGlyated L-asparaginase)	Improved stability of protein through PEGylation, introduction of unique mammalian protein	Chronic gout	2010
Marqibo® (Onco TCS)	Liposomal vincristine	Increased delivery to tumour site, lower systemic toxicity arising from side effects	Acute lymphoblastic leukemia	2012
Ryanodex® (Eagle Pharmaceutical)	Dantrolene sodium Iron oxide	Faster administration	Malignant hypothermia	2014

		at higher doses		
Oniyde® (Merrimack)	Liposomal irinotecan	Increased delivery to tumour site, lower systemic toxicity arising from side effects	Pancreatic cancer	2015
Vyxeos (Jazz Pharma)	Liposomal combination of daunorubicin and cytarabine	Sustained release of the molecules and co-loaded two molecules with synergistic anti-tumour activity	Acute myeloid leuk	

aemia (AML) or AMLA with myelodysplasia-related changes (AML-MRC) 2017

3. CONCLUSION:

Nanocapsules have gained significant popularity in formulation development due to their ability to produce highly precise particles with well-defined biological, electrical, optical, and magnetic properties. The primary techniques used to create these capsules are interfacial nano deposition and polymerization. However, their application is limited to medication delivery systems that require a specific bimolecular triggering action mechanism. These capsules have a wide range of applications across various industries such as agrochemicals, wastewater treatment, genetic engineering, cosmetics, cleaning goods, and adhesive components. They are capable of encapsulating enzymes, adhesives, catalysts, polymers, oils, inorganic micro- and nanoparticles, latex particles, and even living cells. The controlled delivery of active pharmaceutical ingredients (APIs) is one of the significant advantages of using nanocapsules. In the future, the development of nanocapsules will facilitate new and more effective drug delivery technologies.

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