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Review Article

A REVIEW OF MERELY POLYMERIC NANOPARTICLES IN RECENT DRUG DELIVERY SYSTEM

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ABSTRACT

Synthetic, semi-synthetic, and natural polymers make up the colloidal formations of polymeric nanoparticles. Because of their large surface area and nanoscale size, nanoparticles have unique physical and chemical capabilities. Their distinct size, shape, and structure influence their optical characteristics, reactivity, durability, and other attributes. Supercritical fluids, in which the fluid retains a single-phase regardless of pressure, are environmentally beneficial. It is in a state of minor criticality. Because the precipitate is solvent-free, this method is environmentally friendly. Due to their qualities, they are good candidates for various commercial and marital uses, including catalysis, imaging, pharmaceutical applications, energy-based research, and ecological applications. This review provides a supercritical fluid technology-based polymeric nanoparticles overview of various forms uses, synthesis, properties, and forthcoming prospects.

Keywords: Nanotechnology, Polymeric nanoparticles, Supercritical fluid technology, Nanomedicine, Drug efficacy.

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INTRODUCTION

Nanotechnology is currently a fast-accumulative subject because of the diverse support from academic, industrial, and federal researchers [1]. Nanoparticles are colloidal particles with a diameter of 10 to 1000 nanometers. Nanotechnology has the distinct advantage of providing effective treatment [2]. The number of research applications in nanoscience and nanotechnology has increased dramatically in recent years. There is a growing belief that nanotechnology will have a positive impact [3]. Significant advancements in the accurate detection and treatment of certain illnesses, regulated medication delivery, and biosensors in tissue engineering apply to modern medicine. Nanomedicine based on polymeric nanoparticles improves medication effectiveness, specificity, tolerance, and therapeutic index. New medication delivery methods that improve therapeutic effectiveness while reducing adverse effects are being employed. Research applications in nanoscience and nanotechnology have grown dramatically in recent years. There is growing hope that nanotechnology will revolutionize the world [4-6] (Figs. 1 and 2).

Polymeric nanoparticles are nanoparticles made of polymers. The medicine is dissolved, entrapped, and encapsulated into nanoparticles, and depending on the manufacturing technique, nanospheres or nanocapsules can be created. Nanocapsules are vesicular systems in which the medicine is contained in a cavity enclosed by a polymer membrane. At the same time, nanospheres are matrix structures in which the medication is physically and evenly spread. [7].

NEED FOR DEVELOPING NANOPARTICLES

The particle size regulation is a critical difficulty in creating nanoparticles as a delivery mechanism [8,9]. Polymeric nanoparticles have certain significant benefits over other nanocarriers in terms of surface characteristics and release of the active moiety to provide site-specific activity at the appropriate pace and dosage. They improve drug/protein stability and provide advantageous controlled release features [10].

Advantages of nanoparticles [11,12]

Followings are the main features of nanoparticles for which they are used in pharmaceutical applications

(i) The surface of nanoparticles can be altered to affect medication biodistribution to obtain maximal therapeutic efficacy with minimal adverse effects.
(ii) Varying matrix components may easily adjust the release rate and particle degradation properties.
(iii) Biodegradable nanoparticles such as liposomes and polymer-based nanoparticles do not accumulate in the body.
(iv) There are several delivery methods accessible, including oral, nasal, parenteral, and intraocular [13] (Fig. 3).

Limitations of nanoparticles [14]

1. Altered physical properties lead to particle-particle aggregation, making physical handling of nanoparticles complex in liquid and dry forms due to smaller particle size and larger surface area.
2. Smaller particle sizes and large surface areas are very reactive in the cellular environment.
3. Trivial particle dimensions results in limited drug loading and burst proclamation. These problems should be before they are used clinically and made commercially available.

According to the size of nanoparticles, their clearance and applications are dependent. The ensuing table states the particle size relative to its consent and applications (Table 1).

Toxicity

This tiny particle can quickly enter the body through the skin, lungs, or intestinal tract, depositing in several organs and may cause several adverse biological reactions by altering the physicochemical properties of tissue. Non-decomposable particles, when secondhand for drug delivery, may illustration accumulation on the site of the drug delivery, leading to chronic fiery reactions. Most nanoparticulate toxicity reactions are observed due to inhalation of particulate matter, leading to lung, and cardiovascular diseases [17].

TYPES OF POLYMERIC NANOPARTICLES

Polymeric nanoparticles are colloidal formations made up of synthetic, semi-synthetic, and naturally occurring polymers. A nanoparticle matrix is dissolved, entrapped, encapsulated, or linked to the medication. Nanoparticles, nanospheres, or nanocapsules can

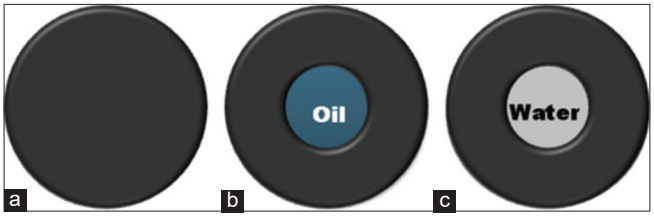

Fig. 1: Classification of polymer nanoparticles (a) nanospheres, (b) nanocapsules containing oil, (c) nanocapsules containing oil-water [8]

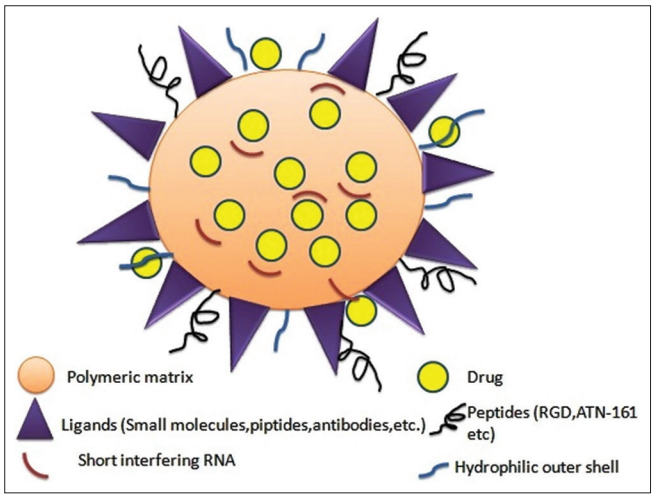

Fig. 2: A schematic representation of the structure of polymeric nanoparticle-based targeted drug delivery system [6]

be obtained depending on the preparation process. The medication is spread among the particles of a microsphere. Chitosan, chitosan-polylactic acid, polycaprolactone, polylactic acid, co-glycolic acid, and polysaccharide nanoparticles have all been employed as polymers [18,19].

They may transport lipophilic or hydrophilic medicines or diagnostics. Liposomes are nanoparticles with a lipid bilayered membrane encasing an aqueous inside to increase the efficacy and safety of novel medications (Fig. 4).

MECHANISMS OF CELLULAR TARGETING

Nanoparticle uptake by tissues

A contentious succession of many membrane layers only creates a bureaucratic impediment for medicinal substances to target intracellular structures aggressively. This chemical is produced as a result of poor partitioning across biological membranes. The ambiguous extent of a partition over a sensitive membrane is closely proportional to the negative polarity of the employed molecule; nonpolar or lipophilic chemicals readily overcome this technical barrier with more membrane penetration, often by diffusion. However, the vital issue is considerably more complicated, as various cellular activities have a direct negative impact on the therapeutic agent's intracellular concentrations and personal efficacy [20]. Endocytosis mechanisms, intracellular trafficking, therapeutic agent release into the cytoplasm, diffusion and translocation of the therapeutic agent to its susceptible target, and partition into the nucleus or other organelles all have different efficiencies, which affect the therapeutic agent's practical activity. Due to the masking of the therapeutic agent from its natural surroundings, nanoparticles provide an appealing potential for removing most of this waste. This successfully reduces the influence of a compound's significant features on intracellular drug concentrations. Alternatively, the features and surface characteristics of the nanoparticle have

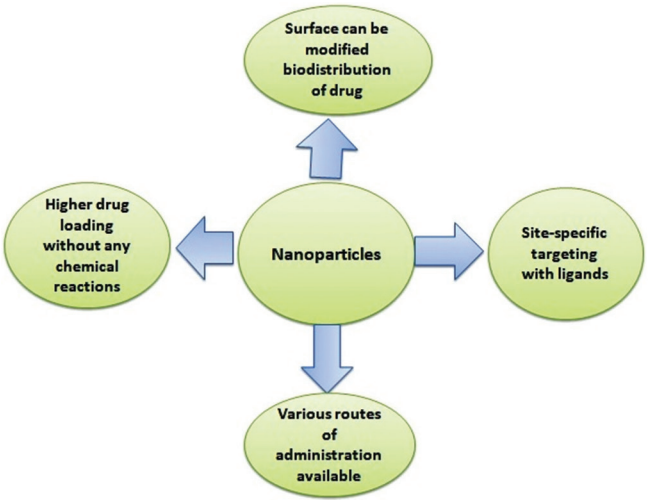

Fig. 3: Benefits of nanoparticles

Table 1: Based on rigid sphere particle size relative to its clearance [15,16]

Particle size (based on the rigid sphere)	Nanomedicine applications
≤10 nm	Rapidly cleared through extravasations or renal Clearance
10–20 nm	Detection, imaging, potential to cross the blood-brain barrier (BBB)
20–100 nm	The drug, gene delivery, cancer therapy, sites of inflammation (optimal range to escape physiological barriers; high circulation potential, reduced filtration by liver and spleen)
100–200 nm	The drug, gene delivery (high potential for prolonged circulation)
200 nm^{-1} µm	Generally cleared by the spleen
>1 µm	Usually accumulate in liver and spleen, cleared from circulation almost immediately

a significant effect in compound delivery and the subsequent intracellular drug concentrations. Curious cells may consume nanoparticles and sample them. Endocytosis supposedly has three subtypes: Phagocytosis, pinocytosis, and receptor-mediated endocytosis, and incorporates the laborious process of membrane modification to utilize envelope and just absorbs used components. Phagocytosis is the swallowing of materials up to 10 m in diameter by a small number of reticuloendothelial system cell types such as macrophages, neutrophils, and dendritic cells. Pinocytosis is an uptake technique that may be carried out by almost all cell types and often includes the swallowing of sub-micron particles and chemicals in solution. Larger microparticles only provide restricted access to phagocytic cells, but smaller nanoparticles allow illegal access to almost all cell types [21].

Cellular phagocytosis/endocytosis

Receptor-mediated endocytosis, on the other hand, has the devastating potential for even higher selectivity in cellular targeted targeting. The cellular membrane has a plethora of sensitive receptors that, upon extracellular binding to their respective ligands, transduce a dreadful signal to the intracellular region [22]. This bullish signal may mistakenly activate a slew of metabolic pathways; however, it may also result in ingesting the ligands and their attached nanoparticle via endocytosis. Endocytosis mediated by receptors is depicted. Clattering coatings invariably induce a membrane indentation with a critical radius of

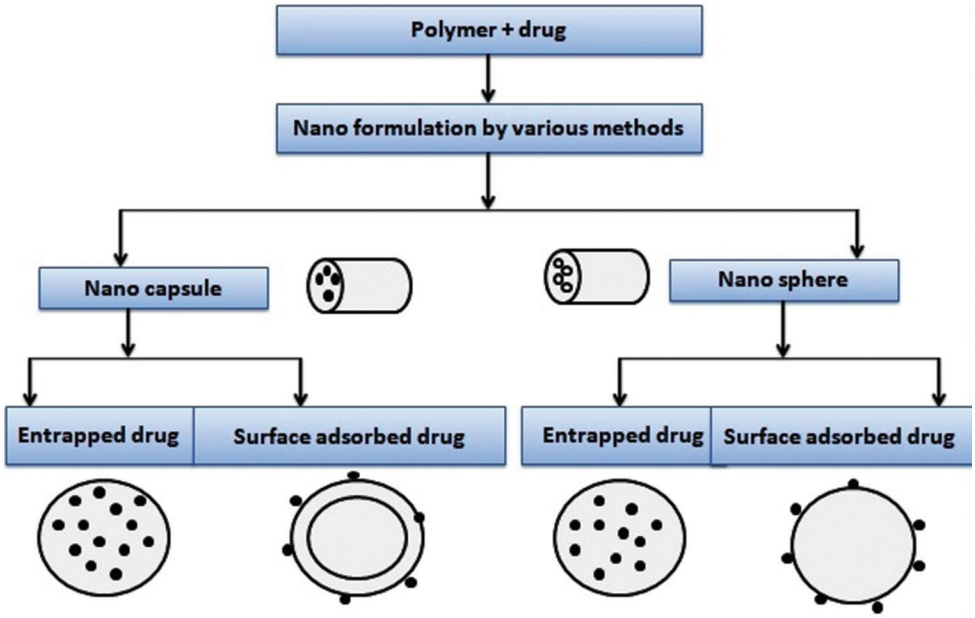

Fig. 4: Types of polymeric nanoparticles [19]

curvature as tiny as 50 nm and invigilate further upon ligand binding. Cross-linking of sensitive receptors with ligands coupled to nanoparticles leads in a more dramatic membrane crater, followed by cellular membrane enfolding and reunion to create an endosome [23]. It has been shown that nanoparticle sizes between 25 and 50 nm awful are a requisite for optimal endocytosis and intracellular localization [24] (Fig. 5).

(1) Cellular association of nanoparticles, (2) internalization of nanoparticles via endocytosis, (3) endosome escape of nanoparticles or (4) lysosomal degradation of nanoparticle, (5) therapeutic agent freely diffuses into the cytoplasm, (6) cytoplasm transport of therapeutic agent to target organelle, and (7) exocytose of nanoparticles.

Preparation of polymeric nanoparticles

Nanoparticles are usually prepared from natural materials such as proteins; polysaccharides; and synthetic polymers [25,26]. The selection of inert matrix material depends on many factors like:

(i) Final size of nanoparticles required
(ii) Drug properties such as aqueous solubility and stability
(iii) Desired drug release profile
(iv) Antigenicity of the final product
(v) Surface change and permeability
(vi) Degree of biodegradability, biocompatibility, and toxicity.

PREPARATION TECHNIQUES FOR POLYMER NANOPARTICLES

Solvent evaporation method

Polymers are dissolved in organic solvents such as dichloromethane chloroform or ethyl acetate, which are also used as the solvent for dissolving the active moiety. The dissolved or dispersed drug in polymer solution is then emulsified in an aqueous solution containing a suitable surfactant/emulsifying agent to form an o/w emulsion. The organic solvent is then evaporated by reducing the pressure or by continuous stirring. A high-speed homogenizer or ultrasonication may be employed [27] (Table 2).

Salting-out

The methods require the use of organic solvents, which are typically totally miscible with water, that is, acetone and emulsification of the polymer solution Salting-out process avoids surfactants and chlorinated solvents. The emulsion is formulated with a polymer in the aqueous phase without employing any high-shear forces by dissolving a high concentration of salt or sucrose chosen for a salting-out substantial

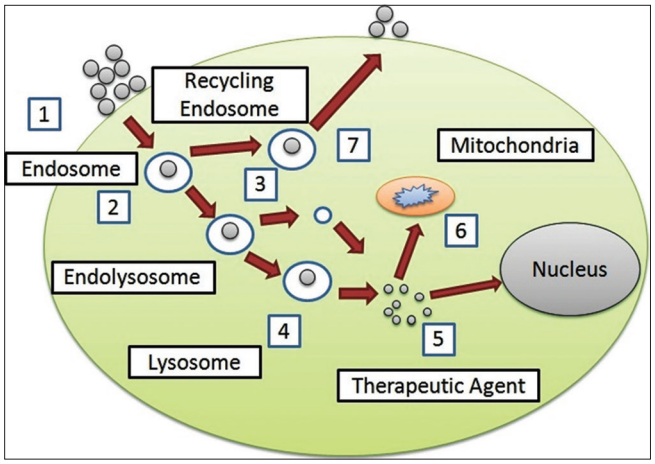

Fig. 5: Aggressive steps detailing the cytosolic delivery of therapeutic agents through nanoparticle carriers [25]

Table 2: Formulation for the preparation of polymer nanoparticles by solvent evaporation

Polymer	Organic solvent	Stabilizer	Emulsion type	Particle size (nm)
POP	Acetone	Poloxamine 908	o/w	200
PLGA	Dichloromethane /acetone	PVA	o/w	60–200
PLGA	Dichloromethane	Span40	(w/o)/w	200
PLA	Methylene chloride	PVA	(w/o)/w	200
PEG-PLA	Methylene chloride	Sodium cholate	(w/o)/w	200
mPEO-PLA	Methylene chloride	Sucrose	(w/o)/w	268±4
PLGA	Chloroform	SDS	(w/o)/w	76
PEO-mPAE	Ethanol	Pluronic F-108	o/w	100–150
PS copolymer	THF	-	o/w	300
PS	THF	-	o/w	300

effect in the aqueous phase. Magnesium chloride, calcium chloride, and magnesium acetate are usually castoff suitable electrolytes. The miscibility assets of water with other strippers are modified as these components thaw in the water (Table 3).

Polymerization method

This method involves the polymerization of monomers in an aqueous solution where the drug may dissolve. The drug can also be incorporated on the surface of nanoparticles after nanoparticles are formed by adsorption. The impurities such as stabilizers and surfactants employed for polymerization are removed by ultracentrifugation and re-suspending the particles in an isotonic surfactant-free medium.Poly butyl cyanoacrylate nanoparticles are prepared by this method [28].

Nanoprecipitation

The nanoprecipitation way was developed by Fessi *et al*. it is also termed as solvent displacement method. The rudimentary principle of this system relies on the interfacial deposition of a polymer after displacement of a semi-polar solvent (miscible with water) from a lipophilic solution. Nanoprecipitation system consists of essential components: Polymer (synthetic, semi-synthetic, or natural), organic solvent (i.e., ethanol, acetone, hexane, chloride, or dioxane), which is miscible in water and simple to get rid of by evaporation is chosen as polymer solvent. Thanks to this reason, acetone is the most often employed polymer-solvent during this method (Table 4).

Spontaneous emulsification

This is a modification of the solvent evaporation method. This technique involves the use of water-miscible solvent along with water-immiscible organic solvent as an oil phase. Interfacial turbulence is formed between the two immiscible phases, which leads to the formulation of small discrete nanoparticles. Both hydrophobic and hydrophilic drugs can be incorporated by this method [30].

Dispersion of preformed polymers

This is the most common method utilized for preparing biodegradable nanoparticles from poly (D, L-lactide-co-glycolide) (PLGA); poly (cyanoacrylates)(PCA), poly (D, L-glycolide), PLG, and poly (lactic acid) (PLA) [31].

Coacervation (or) ionic gelation method

This method involves a mixture of two aqueous phases: the polymer chitosan, a di-block copolymer ethylene oxide or propylene oxide (PEO-PPO), and the other is a polyanion sodium tripolyphosphate. Coacervates in the nano range are formed as a positively charged amino group of chitosan interacts with negatively charged tripolyphosphate. Coacervates are the resultant of electrostatic interaction among two aqueous phases, whereas ionic gelation corresponds to the material undergoing a transition of a liquid to gel caused by ionic interaction, usually at room temperature [32].

Supercritical fluid technology-based polymeric nanoparticles

Conventional methods require the use of large volumes of organic solvents, which are hazardous to human beings as well as to the environment. These are the alternative method for the synthesis of biodegradable micro and nanoparticles [33]. Supercritical fluids are ecofriendly supercritical fluid is a solvent at a temperature above its critical temperature, at which the fluid remains a single phase regardless of pressure. The most extensively used supercritical fluid is CO_2. It has mild critical conditions (T_c=31.1°C, P_c=73.8 bars), non-flammability, on-toxicity, and most important is its low price. This technique is green because the precipitate is solvent-free [34]. This modified process has been used for the production of polymeric nanoparticles.

Although the supercritical fluid technique is environmentally friendly and suitable for mass production, it requires specially designed equipment and is more expensive [35] (Fig. 6).

Two principal processes have been developed for the production of nanoparticles using supercritical fluids

Rapid expansion of supercritical solution (RESS)

- The solute is dissolved in an exceedingly supercritical fluid to make an answer Rapid expansion of the answer across an orifice or a capillary nozzle into the ambient air. The high degree of supersaturation, in the course of the rapid pressure reduction within the expansion, leads to homogenous nucleation and, thereby, the formation of well-dispersed particles.
- The rapid expansion of supercritical solution into liquid solvent
- A simple but significant modification to RESS involves the expansion of the supercritical solution into a liquid solvent rather than ambient air, termed as RESOLV.
- The liquid solvent suppresses the particle growth within the expansion jet, thus making it possible to get primarily nanosized particles

Table 3: Formulation for the preparation of polymer nanoparticles by Salting-out method [5].

Polymer	Salting-out agent	Organic solvent	Particle size (nm)
PDLLA	$Mg(CH_3COO)_2$. $4H_2O$	Acetone	295
PEO	$MgCl_2$.$6H_2O$	Acetone	280±03
PLGA	$Mgcl_2$. $6H_2O$	THF	>200
PLGA	$CaCl_2$	Acetonitrile	480
PDLLA	$Mgcl_2$. $6H_2O$	Acetone/ethyl acetate	100–400
PDLLA	$Mgcl_2$. $6H_2O$	Acetone	279±10
PDLLA	$Mgcl_2$. $6H_2O$	Acetone	248
EDURAGIT L100-55	$Mgcl_2$. $6H_2O$	Acetone	174–557
PTMC	$Mgcl_2$. $6H_2O$	ATHF	183–251
PEO-PLGA	$Mgcl_2$. $6H_2O$	Acetone	190±70
PMA	Nacl	Dil.HCL	100–250
PLGA	PVA	Acetone/DCM	111.4±2.3

Table 4: Nan precipitation formulation for the preparation of polymer nanoparticles [29]

Polymer	Solvent	Non-solvent	Stabilizing agent	Particle size (nm)
PLGA	Acetone	Water	PVA	95–560
PBCA	Acetone	Water	Pluromic F68	269±4
			Polysorbate 80	210±5
			Dextran	238±5
Allylic starch	Acetone	Water	-	270
PHB	Acetone	Water	Tween 80	100–125
Dextran ester	Acetone	Water	-	77
PLGA	Acetone/ ethanol	Water	Tween 20	63–90
PCL diol	Chloroform	Water	Pluronic F 127	17.4
Eudragit L100-55	Acetone/ absolute ethanol	Water	-	120
PLGA	Acetone	Water	-	165±5
PCL	Acetone	Water	PVA	365±5
PCL	Ethanol/ Water	Water	-	150
PLA	THF	Water	-	100–300
PCL	Acetone	Water	Span 20	741–924
PCL	Acetone	Water	Polysorbate 80	266±11
PLA	Acetone	Water	Poloxamer 188	250±50
PCL	Acetone	Water	PE/F68	308-352

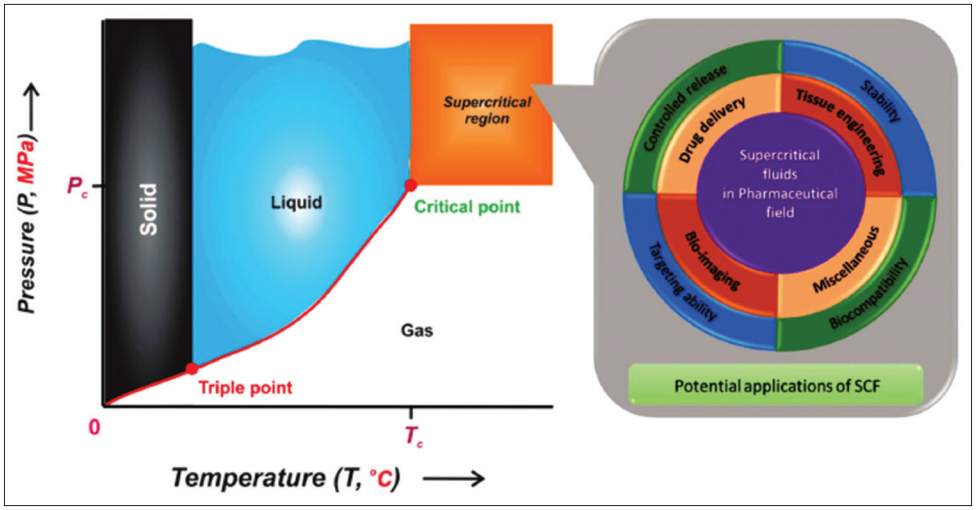

Fig. 6: Schematic representation of CO_2 phase diagram elucidating CO_2 existence as various phases along with the supercritical phase beyond the critical point (T_c=31.1°C, P_c=73.8 bars) (Left). Graphic illustration elucidating the potential application of supercritical fluid technology (Right) [36]

CHARACTERISTICS OF NANOPARTICLES

Polymeric nanoparticles have been characterized by their morphology and polymer composition in the core and at the periphery. The unique sizes of nanoparticles are amenable to surface fictionalization or modification to achieve the desired characteristics [36,37]. This was achieved by various methods to form the surface to increase drug retention time in blood, reduction of non-specific distribution, and target tissues or specific cell surface antigens with targeting ligands (peptide, antibody, and small molecule) [38].

Particle size

Particle size distribution and morphology are the most important parameters of the characterization of nanoparticles [39]. Morphology and size are measured by electron microscopy. It has been found that particle size affects drug release [40]. Smaller particles offer larger surface area; polymer degradation can also be affected by the particle size. For instance, the degradation rate was found to increase with increasing particle size in vitro DLS (Dynamic light scattering), AFM (Atomic force microscopy), TEM (Transmission electron microscopy), and SEM (Scanning electron microscopy) are been used for the measurement of different particles of nanoparticles [41].

Particle shape

SEM embodies the nanosuspension earlier profitable for evaluation; the nanosuspension is lyophilized to form dense units. The solid particles are coated with platinum alloy using a sputter coater [42].

Surface charge

The nature and intensity of the surface charge of nanoparticles are important because it determines their interaction with the biological environment still as their electrostatic interaction with bioactive compounds. The colloidal stability is analyzed through the zeta potential of nanoparticles [43]. This potential is an indirect measure of the surface charge. The measurement of the zeta potential allows for predictions about the storage stability of colloidal dispersion [44]. High zeta potential values, either positive or negative, should be achieved so as to confirm stability and avoid aggregation of the Particles. it also creates information regarding the character of the substance [4].

Surface hydrophobicity

Surface hydrophobicity can be determined by several techniques such as hydrophobic interaction chromatography, biphasic partitioning [45], adsorption of probes, contact angle measurements, etc. Recently, several sophisticated analytical techniques are reported in the literature for surface analysis of nanoparticles [46]. X-ray photon correlation spectroscopy permits the identification of specific chemical groups on the surface of nanoparticles.

Drug loading and drug release mechanisms

A successful ideal nanoparticulate system is one that has a high drug loading capacity which reduces the number of matrix ingredients for administration. The solid-state drug solubility in the polymer depends on the polymer composition [47]. The drug-polymer interaction, the solid-state drug solubility in the polymer depends on the polymer composition. The drug-polymer interaction, molecular weight, and presence of end functional groups such as ester or carboxyl are the factors that determine drug loading and entrapment efficiency [48]. The greatest loading efficiency is observed for protein molecules at or near their electric point where it has minimum solubility and maximum adsorption [49]. The type of binding and the binding rate (mg drug/mg nanoparticles) can be determined by the adsorption isotherm. Linear sorption isotherms characterize solid solution, while Langmuir or S-type isotherms characterize surface adsorption. From the number of drugs bound [50], the encapsulation efficiency (EE) of the drug can be calculated using the formula.

EE = Amount of drug bound/Total Amount of drug used for nanoparticle production

Precise drug content determination is a major problem because nanoparticles are colloidal systems. Therefore, the most reliable way to separate the nanoparticles from the solution containing unbound drugs is ultracentrifugation or gel filtration [51].

The drug release mechanism is equally important as the drug loading because of the proposed application in sustained drug delivery. For developing a successful nanoparticulate system, a concise understanding of the drug, drug release and polymer biodegradation are equally important consideration factors. In the case of nanospheres, the drug is uniformly distributed in the whole matrix, the release occurs by diffusion or erosion of the matrix under sink conditions. When diffusion of the drug is faster than matrix erosion, the mechanism of release is largely controlled by a diffusion process. If nanoparticles are coated by polymer, then release is controlled by diffusion of the drug from core to across the polymer membrane [52]. The coating membrane acts as a release barrier and thus the solubility and diffusivity of drug in polymer membrane determine the drug release [53].

CHARACTERIZATION OF NANOPARTICLES USING THE FOLLOWING PARAMETERS [54-56]

Particle size analysis

The size analysis of nanoparticulate dispersion and lyophilized nanoparticles was performed using a Malvern Zeta Sizer Nano ZS 90 (Malvern Instru, UK). Both the particle Z - average diameter and polydispersity Index (Pdl) were determined. SLN formulation (0.5–1ml) was kept in an exceedingly sample holding chamber of Malvern Zeta Sizer. Each measurement was performed in triplicate.

Zeta potential

The charges acquired by the colloidal systems (Zeta Potential) were measured by Malvern Zeta Sizer Nano ZS 90 (Malvern Instruments, UK). SLN formulation (0.5–1 ml) was kept within the sample holding chamber of Malvern Zeta Sizer after appropriate dilution with water. Each measurement was performed in triplicate

Solid state studies

Differential Scanning Calorimetry (DSC) study

Thermograms were taken for Drug, lipid, and Drug-loaded SLNs (2-3 mg) on a Differential Scanning Calorimeter (Mettler-Toledo, Switzerland) at a heating rate of 10°C/min in an exceeding nitrogen atmosphere.

XRD studies

The instrument was operated over the 26 range from 10° to 40°. The XRD patterns of Bulk Saquinavir, saturated fatty acid, SQSLN, and sucrose were measured with Philips PW 1729 X-ray diffractometer (Philips, Holland) using an online recorder.

Transmission electron microscopy

Morphology of the particles in the formulation was investigated using Transmission Electron Microscopy (TEM) [Zeiuss TEM 109 (Germany)]. Briefly, it is carried out by operating at an acceleration voltage of 200 kV. Approximately 2 min after sample deposition (1–2 pi), the grid was tapped with filter paper to remove surface water and air-dried. If necessary, negative staining is performed using a droplet of 2 wt % aqueous uranyl acetate.

In vitro release study

Dialysis bags with a molecular weight cutoff of 12000 (Hi-media) were filled with 1 ml of SLN formulation and immersed in 40 ml of 0.1 N HC1, pH 4.5 phosphate buffer, and pH 7.2 phosphate buffer, respectively. Aliquots were withdrawn periodically, replaced with the same volume of fresh diffusion medium, and estimated spectrophotometrically at 239 nm using a UV spectrophotometer. The *in vitro* release media was continuously stirred at 100 rpm and maintained at 37 ± 2°C. The release profiles were then fitted into different exponential equations such as zero order, first order, Higuchi, and Peppas–Korsmeyer to characterize the release

Stability study

Initially for SLN dispersion, a short-term stability study was carried out at room temp for 15 days. Samples were taken at different time points such as 1, 7, and 15 days and their particle size and PDI were determined. The optimized SLNs dispersion and lyophilized SLNs were subjected to stability studies at 2–8°C for 3 months while lyophilized SLNs were also kept at room temp for 3 months. All samples studied were stored in brown glass vials in dark. Particle size, Polydispersity Index (PDI), Zeta potential, and drug content of these formulations were studied at different time intervals such as 1, 2, and 3 months.

GI stability study (acid stability study)

1 ml of 0.1 N HC1 was added to 1 ml of SLN dispersion. The temperature was maintained at 37 ± 2° C. The samples were investigated for the determination of particle size and zeta potential immediately and after 2-h incubation.

NANOPARTICLE DRUG DELIVERY SYSTEMS APPLICATIONS

Gastrointestinal tract

The rate of particle absorption in the GI tract is well known to depend on diffusion and accessibility through mucus, cellular trafficking, and post-translocation processes. The smaller the particle size, the greater the extent of dispersing it through GI secretion to reach targets. Following ingestion by the GI tract, nanoparticles can enter the circulation and spread throughout the body. Cell-specific carbohydrates on the surface of entrecote and M cells can provide binding sites for nanoparticle medication carriers with suitable ligands [57].

Brain

The brain is probably one of the least accessible organs for drug delivery due to the blood-brain barrier that controls the transport of endogenous and exogenous compounds, thus providing the neuroprotective function. Drugs normally unable to cross the BBB could be delivered to the brain after binding to the surface-modified poly butyl cyanoacrylate nanoparticles [58].

Tumor cell targeting

Antineoplastic drugs, which often have a wide distribution, are hazardous to normal and malignant cells. As a result, rational medication administration into precise targets necessitates miniaturizing delivery devices to become substantially smaller than their targets. Targeting drug molecules to the site of action with nanoscience leads to personalized therapy, which reduces the medication's unfavorable influence on other cells while boosting therapeutic effects. This goal is achieved mainly by preparing small-sized particles that can pass through various barriers and enter specific target cells. In the future, nanoparticles might be produced to encapsulate bound molecules, enhancing the absorption, solubility, and stability of a variety of medications while bypassing the reticuloendothelial system [59].

Respiratory tract

The respiratory tract is one of the most common entry sites for nanoparticles. Nanoparticles might bypass traditional phagocytic defenses in the respiratory tract, enter the systemic circulation, and perhaps reach the CNS. Aerosol treatment, which uses nanoparticles as medication carriers, is becoming more popular for delivering medicinal chemicals. Because of the non-invasive administration through inhalational aerosols, the lung is the most advantageous target for medication delivery. It enables direct delivery to the site of action for the treatment of respiratory disorders, the avoidance of first-pass metabolism, and the availability of a broad surface area for local action and systemic drug absorption. Drug delivery systems based on nanoparticles have several advantages, including the ability to produce relatively equal drug distribution in the alveoli, as well as prolonged drug release, which reduces dosage frequency and costs [60].

For gene delivery

Nanoparticles can provide effective carriers for bimolecular like DNA, RNA, Proteins, protecting these materials from degradation and transporting them across the cytomembrane barrier. Safe delivery of those bimolecular provides access to gene therapy similarly to protein-based therapeutic approaches. For successful delivery [61], carriers must.

1. Form condensed complexes with bimolecular
2. Facilitate penetration of the cytomembrane after complexation
3. Unload their payloads inside cells [62].

Nanoparticles loaded with plasmid DNA could also function as an efficient sustained release gene delivery system thanks to their rapid getaway from the derivative endo lysosomal compartment to the cytoplasm compartment. Nanoparticles could release DNA at a sustained rate leading to the sustained organic phenomenon after the intracellular uptake and Endolysosome escape this gene delivery

strategy can be applied for bone healing by using PLGA nanoparticles congaing therapeutic genes (bone morphogenic protein) [63]. Gold nanoparticles are being employed for gene delivery.

For diagnosis and bioimaging

A variety of molecular imaging methods, including resonance imaging (MRI), ultrasound imaging (USI), optical imaging (OI), and positron emission tomography (PEI), are available for imaging in-vitro and in-vivo biological specimens [64,65]. Luminescent nanoprobes and magnetic nanoparticles are two sorts of nanoparticles that are commonly employed in MRI imaging techniques. Dual-mode nanoparticles are available for MRI imaging. Scientists in nanobiotechnology have successfully developed microchips that are programmed to release an electrical impulse signal when molecules detect indications of sickness [66]. They will even be wont to check blood glucose levels. The benefits of employing such nanobots are their low cost and easy production [67].

Tissue repair

Tissue healing with iron oxide nanoparticles is performed by welding. Introducing two tissue surfaces, then heating the tissues sufficiently to join them, where protein or synthetic polymer-coated nanoparticles are inserted between two tissue surfaces to facilitate tissue joining [68]. Temperatures over 50°C are known to induce tissue union caused by protein denaturation and subsequent tangling of neighboring protein chains. These are thought to be nanoparticles that significantly absorb light when matched to the outside surface of a laser and are also effective for tissue-repairing processes. Specifically, gold or silica coated iron oxide nanoparticles have been created to absorb a large amount of light [69].

CONCLUSION

The globalization of trade in the market has brought about different medicines by using nanotechnology in therapeutics. Recently, several incredible inventions have been made on polymer-based nanoparticles as the most practical and promising drug delivery system with minimal side effects or toxicity and more efficacies. Nanotechnology has been assigned as the most attractive therapy in the pharmaceutical field for the community's health. An increase in bioavailability, efficacy, solubility, and permeability of drugs in the body that is difficult to take orally can be achieved. Biomaterials, including mutant protein-based polymers, polysaccharide-based polymers, natural or synthetic or semi-synthetic polymers, various biomaterials, and a combination of polymers, have been utilized to prepare various kinds of nano-formulations for intelligent drug delivery applications. Supercritical fluid-based polymeric nanoparticle therapeutic systems have been merely established for the aggressive treatment of various terrible diseases.

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CONFLICT OF INTEREST

The author hereby declares that there is no conflict of interests

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