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A COMPREHENSIVE REVIEW ON POLYMERIC NANO PARTICLES

Anita Sharma, Sameer PMD*

Shree Venkateshwara College of Paramedical Sciences College of Pharmacy, Gobichettipalyam, Tamil Nadu, India

Correspondence
Sameer PMD *
Shree Venkateshwara College of Paramedical Sciences, College of Pharmacy, Gobichettipalyam, Erode, Tamil Nadu, India
✉ sameermohamad1995@gmail.com

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ABSTRACT

Nanotechnology is the most promising and pioneer technique in the health care system. A Nano pharmaceutical product overcomes the limitation of conventional chemotherapy. In recent trends, it is found to be more effective and safer for the treatment of various chronic diseases such as cancer. Nano-sized drug shows better reachability to the target site with enhanced performance as of their high surface area. The site-specific drug delivery, biocompatibility, biodegradability, conjugation, encapsulation, and fictionalization of Nanosized drugs make it a potential candidate in the drug delivery system. Multiple types of nano products are used. Polymeric Nanoparticles have been proved to be a more suitable carrier for drug delivery and thereby increasing the drug safety profile; these polymeric Nanoparticles can transport various biomolecules and synthetic molecules ranging from DNA, Proteins to Drug Molecules to the target organ. This review article focuses on the application of nanotechnology, different types of nano products, a brief introduction about polymeric nanoparticles, preparation of nanoparticles, and its evaluation.

INTRODUCTION

Nanotechnology can be defined as the process of designing, characterizing, production of devices, systems by controlling their size and shape at the nanometer range. Various characteristics and brief applications of Nano-systems are described briefly in table.1.

The term nanotechnology is originated from the Greek word 'Nanos' which means dwarf. Nano pharmaceutical scale ranges from 1 - 100 nm which could be increased up to 1000 nm. The nano-size of the drug particle has high surface area and can reach the targeted site because it's extremely small size and small size enhances the performance in a range of dosage forms.

Nano preparation is chosen for the characteristics such as biocompatibility, biodegradability, conjugation, encapsulation, or complexation and their ability to be functionalized.[1] Nano preparations as drug delivery carriers are made in such a form that they can carry a high amount of chemotherapeutic agents into the cancerous cells while sparing healthy cells. Nano Particles have changed the approaches in the oncology field because of their ability of cancer cell-specific targeting and also showing sustained drug release by overcoming the traditional chemotherapy limitations.[2]

Applications of Nanotechnology in the medical field

- Used in targeted drug delivery (therapy) to brain and cancer therapy
- drug delivery and
- Bio detection of pathogen
- Detection of proteins
- Biomarker mapping
- Probing of DNA structure
- Tissue engineering

- By heating process destruction of tumors (hyperthermia)
- Separation and purification of biomolecules and cells
- MRI contrast enhancement.
- Phago-kinetic studies.

Anti-cancer drug in the form of Nanoparticles

One of the major applications of nanoparticles is as the delivery of different anticancer drugs The structure and tunable surface functionality of nanoparticles allows for the encapsulation/Conjugation of multiple entities, either in the core or on the surface, The idea behind using NPs for cancer cell targeting is based on (1) NPs are capable of delivering a fixed-dose active drug molecule to the tumor targets (2) NPS will reduce the drug exposure of health tissues by limiting drug distribution to the target organ. [3]

Oral drug delivery by nanoparticles

The NPS is assumed to protect certain drug which is sensitive towards enzymatic degradation in the GI tract caused to develop NPs for Oral delivery systems. The GI tract provides a range of physiological and anatomical barriers against protein or peptide delivery, e.g., (a) Photolytic enzymes in the gut lumen like pepsin, trypsin, and chymotrypsin; (b) photolytic enzymes at the brush border membrane (endopeptidases); (c) bacterial gut flora; and (d) mucus layer and epithelial cell lining itself. Bioactive molecules are encapsulated by a polymeric nanoparticle which provides protection from hydrolytic and enzymatic degradation

Nanoparticles as a Carrier of Anticancer Drug

One of the major applications of nanoparticles is as a delivery vehicle for various anticancer drugs. The structure and tunable surface functionality of NPs allows for the encapsulation/conjugation of multiple entities, either in the core or on the surface, rendering them ideal carriers for various anticancer drugs. The idea behind using NPs for cancer cell targeting is based on (1) NPs are capable of delivering a fixed dose of drug to the tumor targets (2) NPs will reduce the drug exposure of health tissues by limiting drug distribution to target organ. [4]

Nanoparticles for Oral Delivery

The Nps are assumed to protect certain drugs which are sensitive towards enzymatic degradation in GI tract caused to develop NPs for Oral delivery systems. The GI tract provides a range of physiological and anatomical barriers against protein or peptide delivery, e.g., (a) Photolytic enzymes in the gut lumen like pepsin, trypsin, and chymotrypsin; (b) photolytic enzymes at the brush border membrane (endopeptidases); (c) bacterial gut flora; and (d) mucus layer and epithelial cell lining itself. A polymeric nanoparticle facilitates encapsulation of bioactive molecules and provides protection against enzymatic and hydrolytic degradation. [5]

NANO PHARMACEUTICAL PRODUCTS

Nano Engineered Products

a) Nanoparticles,
b) Nano suspension,
c) Nano emulsion,
d) Nano gels, etc.

The above mentioned pharmaceutical dosage forms are those which contain drug-loaded Nanoparticles.

Nano carrier Products

A. Polymeric Nano carriers

1. Polymeric nanoparticles
2. Polymeric micelles
3. Dendrimers
4. Polymeric hydrogels
5. Polymer-drug conjugates

B. Lipid-based Nano carriers

1. Liposomes
2. Solid lipid nanoparticles
3. Phospholipid micelles
4. Nano emulsions
5. Self-emulsifying drug delivery systems

C. Inorganic Nano carriers

1. Quantum dots
2. Gold nanoparticles
3. Magnetic nanoparticles
4. Silica nanoparticles
5. Carbon nanotubes

Nano carriers can be defines as colloidal particulate systems that have a size ranging between 10-1000 nm. They are utilizing for diagnosis, treatment, and monitoring of different diseases. Figure 1 gives a representation of different types of Nano carriers. [6]

Nanoparticles

The particles have size <100 nm in diameter can be defined as nano-particles.

Advantages of nanoparticles

Nanoparticles have many significant advantages over conventional and traditional drug delivery systems.

- They include Nanoparticles offer sustained and controlled drug delivery at the site of action

- Nanoparticles can be administered by different routes in the body
- In small areas of the body, NPs show better drug delivery when compared to other conventional drug delivery methods as they can easily target a specific cell or a receptor.
- Due to nanoparticle size NPs can overcome the resistance of physiological barriers of body and easily pass the cell wall, blood vessels, blood-brain barrier and stomach epithelium also.
- Nanoparticle enhances the aqueous solubility of the poorly soluble drugs, which improves bioavailability of the drug.
- As a targeted drug delivery system nanoparticles can reduce drug toxicity and enhances efficient drug distribution [7].
- Polymers are used to modify drug release from nanoparticles which make nanoparticles useful for cancer therapy, contraceptives and vaccines [8].

Limitations of Nano particles

There have been various limitations reported for NPs even though they are having many advantages.

1. Limitations make scientist to work more on side effect free or with lesser side effect nanoparticle which can show potent therapeutic effect [9].
2. Smaller particle size and larger surface area change the physical properties which lead to aggregation of particles in liquid and dry forms. In cellular environment nanoparticle are very reactive due to its small particle size and larger surface area [10-11].

POLYMERIC NANOPARTICLES (PNPs)

The polymeric nanoparticles are generally formulated by using biodegradable and biocompatible polymers of size range in between 10-1000 nm, where the drug molecule is made to easily dissolve, entrap, encapsulate or attach to a nanoparticle matrix also be obtained. Nanoparticles, nano capsules/ nano spheres preparation is depend upon the method use for it. Poly membrane surrounded cavity in which the drug molecules are fixed is called nano capsules, matrix systems where the drug is physically and uniformly dispersed is called nano spheres [12-13]. Polymeric nanoparticles are the good carrier by easiliy manipulation which makes an adwantage to impove drug safety [14].

Polymer-based nanoparticles are effective in carrying drugs, proteins and biomolecules to specific target cell. Nano size of drug facilitates the easy penetration of drug in the cell membrane and stability in the systemic circulation. A schematic diagram represents how polymeric nanoparticles are synthesized are is shown in figure 2.

Name of polymer used (for preparation of polymeric Nanoparticles)

1. Nontoxic, non-antigen forming and body compatible polymers should be used in formulation of Polymeric Nanoparticles, it must be biocompatible and biodegradable [15].
2. Natural and synthetic origin Polymers can be used.

Natural polymers [16-18]

In the preparation of polymeric nanoparticles commonly used natural polymers are

- Albumin
- Chitosan
- Sodium alginate
- Gelatin

Synthetic polymers [19-21]

- Poly acrylic acid
- Poly lactides (PLA)
- Poly (vinyl alcohol)
- Poly glycolides (PGA)
- Poly(methyl methacrylate)
- Poly(lactide co-glycolides)
- Poly N-vinyl pyrrolidine
- Poly anhydrides
- Polyorthoesters
- Poly malic acid
- Poly cyanoacrylates
- Poly glutamic acid
- Poly caprolactone

Mechanisms of Drug Release [15]:

The polymeric coated drug Nanoparticles carries the drug to the tissue site by any one of the 3 Physico-Chemical mechanisms.

- By the swelling of the polymer nanoparticles by hydration which is followed by release of drug through diffusion.
- By an enzymatic reaction which results in rupture or cleavage or degradation of the polymer at the site of delivery, there by releasing the drug from the entrapped inner core.
- Dissociation of the drug from the polymer and its de-adsorption/release from the swelled nanoparticles.

Techniques of preparation

The properties of Polymeric Nanoparticles have to be optimized according to its application.

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Methods for preparation of nanoparticles from dispersion of preformed polymer.

Dispersion of drug in preformed polymers is a common technique used to prepare biodegradable nanoparticles. These can be accomplished by different methods described below.

a) Solvent evaporation
b) Nano precipitation
c) Emulsification/solvent diffusion
d) Salting out
e) Dialysis
f) Supercritical fluid technology (SCF)

Methods for preparation of nanoparticles from polymerization of monomers

a) Emulsion
b) Mini emulsion
c) Micro emulsion
d) Interfacial polymerization
e) Controlled/Living radical polymerization(C/LRP).

Ionic gelation or co-acervation of hydrophilic polymers

Solvent evaporation method

The first developed methods for preparation of nanoparticles was Solvent evaporation method [26]. The method involves dissolving the polymer in an organic solvent such as dichloromethane, chloroform or ethyl acetate which is also used as the solvent for dissolving the hydrophobic drug. The mixture of polymer and drug solution is then emulsified in an aqueous solution containing a surfactant or emulsifying agent to form oil in water (o/w) emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by reducing the pressure or by continuous stirring. Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration [22].

In order to produce small particle size, often a high-speed homogenization or ultra-sonication may be employed. Afterwards, the solidified nanoparticles can be collected by ultracentrifugation and washed with distilled water to remove additives such as surfactants. Finally, the product is lyophilized. [23] PLGA nanoparticles of about 200nm were prepared by utilizing dichloromethane 1.0% (w/v) as the solvent and PVA or Span 40 as the stabilizing agent. Schematic representation of the solvent-evaporation technique is shown in the figure 3.

Nano precipitation:

Nano precipitation is also called as solvent displacement or interfacial deposition method, which was first developed and introduced by Fessi's group [31] .The principle of this fabrication method is known as Marangoni effect [24]

In the nano precipitation method, the nanoparticles are obtained in the colloidal suspension when the oil phase is slowly added to aqueous phase under moderate stirring. Formation of the Nanoparticles is instantaneous and needs only one step so it has the advantage of rapid and easy operation. The key parameters in the fabrication procedure have great influence on the Nano precipitation method, such as organic phase injection rate, aqueous phase agitation rate and the oil phase/aqueous phase ratio [25].

Particle sizes of very narrow distribution can be synthesized because of the absence of shearing stress. This method is used mostly for hydrophobic drug entrapment [34], but it is also employed sometimes to incorporate hydrophilic drugs [26]. Polymer and drug are dissolved in a water miscible organic solvent, for example, acetone or methanol. The solution is then added into an aqueous solution which contains surfactant in a drop-wise manner. Through rapid solvent diffusion, the NPs are formed immediately. After that, the solvents are removed under reduced pressure. Tamizhrasi et al, prepared Lamivudine loaded nanoparticles. Firstly drug was dissolved in water and then co solvent (acetone used for make inner phase more homogeneous) was added into this solution. Then another solution of polymer (ethyl cellulose, eudragit) and propylene glycol with chloroform prepared, and this solution was dispersed to the drug solution. This dispersion was slowly added to 10 ml of 70% aqueous ethanol solution. After 5 minutes of mixing, the organic solvents were removed by evaporation at 35°C under normal pressure, nanoparticles were separated by using cooling centrifuge (10000 rpm for 20 min), supernatant were removed and nanoparticles washed with water and dried at room temperature in a desiccator[27]. Schematic representation of the Nano precipitation technique is shown in the figure 4.

Emulsification/solvent diffusion (ESD)

This is a modified version of solvent evaporation method. The encapsulating polymer is dissolved in a partially water soluble solvent such as propylene carbonate and saturated with water to ensure the initial thermodynamic equilibrium of both liquids.

In fact, to produce the precipitation of the polymer and the consequent formation of nanoparticles, it is necessary to promote the diffusion of the solvent of the dispersed phase by dilution with an excess of water when the organic solvent is partly miscible with water or with another organic solvent in the opposite case. Subsequently, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and the formation of Nano spheres or Nano capsules, according to the oil-to-polymer ratio. Finally, the solvent is eliminated by evaporation or filtration, according to its boiling point.

This technique presents several advantages, such as high encapsulation efficiencies (generally >70%), no need for homogenization, high batch-to-batch reproducibility, ease of scale-up, simplicity and narrow size distribution. Disadvantages of this method are the high volumes of water to be eliminated from the suspension and the leakage of water-soluble drug into the saturated-aqueous external phase during emulsification, reducing encapsulation efficiency. As with some of the other techniques, this one is efficient in encapsulating lipophilic drugs [29]

Several drug-loaded nanoparticles were produced by the ESD technique, including

- Mesotetra (hydroxyphenyl) porphyrin loaded PLGA (p-THPP) nanoparticles[30]
- Plasmid DNA-loaded PLA nanoparticles[42]
- coumarin loaded PLA nanoparticles[43]

Schematic representation of the emulsification/ solvent diffusion technique is shown in the figure.5.

Salting out

Salting out is based on the separation of a water miscible solvent from aqueous solution via a salting out effect. The salting out procedure can be considered as a modification of the emulsification/solvent diffusion.

Polymer and drug are initially dissolved in a solvent such as acetone, which is subsequently emulsified into an aqueous gel containing the salting-out agent (electrolytes, such as magnesium chloride, calcium chloride, and magnesium acetate, or non- electrolytes such as sucrose) and a colloidal stabilizer such as Polyvinylpyrrolidine or hydroxyethylcellulose. This oil/water emulsion is diluted with a sufficient volume of water or aqueous solution to enhance the diffusion of acetone into the aqueous phase, thus inducing the formation of Nano spheres [31].

The selection of the salting out agent is important, because it can play an important role in the encapsulation efficiency of the drug. Both the solvent and the salting out agent are then eliminated by cross-flow filtration. This technique used in the preparation of PLA, poly (methacrylic) acid, Nano spheres. It leads to high efficiency and is easily scaled up.

The main advantage of salting out is that it minimizes stress to protein encapsulant [32]. Salting out does not require an increase of temperature and therefore, may be useful when heat sensitive substances have to be processed [46]. The greatest disadvantages are exclusive application to lipophilic drugs and the extensive nanoparticle washing steps [33]. Schematic representation of the salting out technique is shown in the figure.6.

Dialysis

Dialysis offers a simple and effective method for the preparation of small, narrow-distributed PNs [32]. Polymer is dissolved in an organic solvent and placed inside a dialysis tube with proper molecular weight cut off. Dialysis is performed against a non-solvent miscible with the former miscible. The displacement of the solvent inside the membrane is followed by the progressive aggregation of polymer due to a loss of solubility and the formation of homogeneous suspensions of nanoparticles. The mechanism of PNP formation by dialysis method is not fully understood at present. It is thought that it may be based on a mechanism similar to that of nano precipitation

Chronopoulou *et* al [34] reported a novel osmosis based method for the preparation of various natural and synthetic PNP. It is based on the use of a physical barrier, specifically dialysis membrane or common semi permeable membranes that allow the passive transport of solvents to slow down the mixing of the polymer solution with a non-solvent; the dialysis membrane contains the solution of the polymer. A schematic representation of the dialysis technique is shown in the figure 7

Supercritical fluid technology

The need to develop environmentally safer methods for the production of PNP has motivated research on the utility of supercritical fluids as more environmental friendly solvents, with the potential to produce PNPs with high purity and without any trace of organic solvent[35].

Supercritical fluid and dense gas technology are expected to offer an interesting and effective technique of particle production, avoiding most of the drawbacks of the traditional methods. Two principals have been

developed for the production of nanoparticles using supercritical fluids:

a. Rapid expansion of supercritical solution (RESS)
b. Rapid expansion of supercritical solution into liquid solvent (RESOLV).

a) Rapid expansion of supercritical solution [RESS]: In traditional RESS, the solute is dissolved in a supercritical fluid to form a solution, followed by the rapid expansion of the solution across an orifice or a capillary nozzle into ambient air. The high degree of super saturation, accompanied by the rapid pressure reduction in the expansion, results in homogenous nucleation and thereby, the formation of well-dispersed particles. Results from mechanistic studies of different model solutes for the RESS process indicate that both nanometer and micrometre-sized particles are present in the expansion jet [36]

b) Rapid expansion of supercritical solution into liquid solvent [RESOLV]: Even though in RESS technique no organic solvents used for the formation of PNPs, the prime products obtained using this technique are micro scaled rather than nano scaled, which is the main drawback of RESS. In order to overcome this drawback a new supercritical fluid technology known as RESOLV has been developed. In RESOLV the liquid solvent apparently suppresses the particle growth in the expansion jet, thus making it possible to obtain primarily nanosized particles Meziani et al[37].,2004 reported the preparation of Poly (heptadecafluorodecyl acrylate) nanoparticles having an average size of less than 50 nm.

Ionic gelation co-acervation of hydrophilic polymers: Chitosan nanoparticles are mostly prepared using ionic gelation technique. Ionic gelation method has attracted considerable attention, since this method is non- toxic, free from organic solvent, convenient and controllable. Ionic gelation technique is based on the ionic interaction between the positively charged primary amino group of chitosan and the negatively charged groups of polyanion such as sodium tripoly phosphate (TPP), which is the most extensively used ion cross linking agent due to its non-toxic and multivalent properties.

This technique offers a simple and mild preparation method in the aqueous environment. First, chitosan can be dissolved in acetic acid in the absence or presence of stabilizing agent, such as poloxamers, Tween80 which can be added in the chitosan solution before or after the addition of polyanion. Polyanion such as TPP (sodium tripolyphosphate) was then added and nanoparticles were spontaneously formed under mechanical stirring at room temperature. The material undergoes transition from liquid to gel phase due to interaction due to ionic interaction conditions at room temperature. A schematic representation of ionic gelation technique is shown in the figure.8.

EVALUATION PARAMETER OF NANOPARTICLES

Yield of Nanoparticles

The yield of nanoparticles was determined by comparing the whole weight of nanoparticles formed against the combined weight of the copolymer and drug [56].

$$\%\text{yield of nanoparticles} = \frac{\text{amount of nanoparticle}}{\text{amount of drug+polymer}} \times 100$$

Loading Efficiency

Drug loading capacity of the nanoparticles is defined as the amount of drug bound per mass of polymer or in another term it is the moles of drug per mg polymer or mg drug per mg polymer or it could also be given as percentage relative to the polymer. Various techniques such as UV spectroscopy or high performance liquid chromatography (HPLC) after ultracentrifugation, ultra filtration, gel filtration, or centrifugal ultra-filtration are used to determine this parameter. The loading efficiency (L) of the nanoparticles was calculated according to Equation

$$L\ (\%) = (Qn\ /Wn) \times 100$$

Where Wn is the weight of the nanoparticles and Qn is the amount of drug present in the nanoparticles

Zeta potential

The Zeta potential of a nanoparticle is commonly used to characterize the surface charge property of nanoparticles. It reflects the electrical potential of particles and is influenced by the composition of the particle and the medium in which it is dispersed. Nanoparticles with a zeta potential above (±) 30 mV have been shown to be stable in suspension, as the surface charge prevents aggregation of the particles.

Particle size

Particle size and **size distribution are the most** important characteristics of nanoparticle systems. They determine the in vivo distribution, biological fate, toxicity and targeting ability of nanoparticle system. In addition, they can also influence the drug loading, drug release and stability of nanoparticles. Currently, the faster and most routine method of determining particle size is by photon-correlation spectroscopy or dynamic

light scattering. The results obtained by photon-correlation spectroscopy are usually verified by scanning or transmission electron microscopy (SEM or TEM) [38].

Polydispersity index

Polydispersity index is a parameter to define the particle size distribution of nanoparticles obtained from photon correlation spectroscopic analysis. It is a dimensionless number extrapolated from the autocorrelation function and ranges from a value of 0.01 for mono dispersed particles and up to values of 0.5-0.7. Samples with very broad size distribution have polydispersity index values > 0.7[39]

Surface Morphology

Scanning electron microscope is used for surface morphology of prepared nanoparticles for the characterization; dry power should be made from the nanoparticle solution. Power is mounted in sample holder and coated with conductive metal by using sputter coater. The secondary electrons emitted from the sample surface give the surface characterization of the sample. With stand in vacuum condition is mandatory for nanoparticles, and electron beam can damage the polymer.

Kinetic study

The estimation of the kinetics and drug release mechanism carried out by various kinetic equation which are Zero order (cumulative% release v/s time), first order (log% drug remaining v/s time), Higuchi's model (cumulative% drug release v/s square root of time), r^2 and K values were calculated for the linear curve obtained by regression analysis of the above plots [40].

Nanoparticle stability

Storing the prepared and optimized nanoparticle formulation in stability chamber at 40c±10c and 300c±20c determine the stability of nanoparticles. sample formulation were analyzed after a time period at0,1,2 and 3 months for the estimation of their drug content, drug release rate as well as any other changes in their physical appearance (ICH Q1A (*R*2) 2003)

CONCLUSION

Conventional chemotherapy kills not only the cancerous cells but also the healthy ones, which results in very strong side-effects. This significantly hampers the maximum administration of chemotherapeutic drugs. Moreover, short half-life and rapid plasma clearance requires the administration of a high amount of active drug which is costly and often leads to undesirable toxicity effect. Hence novel drug delivery methodologies are developed and employed for the effective treatment of various kinds of diseases. These methods decrease the dose frequency (through controlled and sustained drug delivery) and improve patient compliance.

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REVIEW TABLE AND FIGURE

Table.1.Various Characterization Tools and Methods for Nanoparticles [61]

PARAMETER	CHARACTERIZATION METHOD
Carrier-drug interaction	Differential scanning calorimetry
Charge determination	Laser Doppler Anemometry Zeta potentiometer
Chemical analysis of surface	Static secondary ion mass spectrometry Sorptometer
Drug stability	Bioassay of drug extracted from Nanoparticles Chemical analysis of drug
Nanoparticle dispersion stability	Critical flocculation temperature (CFT)
Particle size and distribution	Atomic force microscopy Laser defractometry Photon correlation spectroscopy (PCS) Scanning electron microscopy Transmission electron microscopy
Release profile	In vitro release characteristics in physiologic and sink situations
Surface hydrophobicity	Rose Bengal(dye) binding Water contact angle measurement X-ray photoelectron spectroscopy

Figure.1. Different Nano carriers

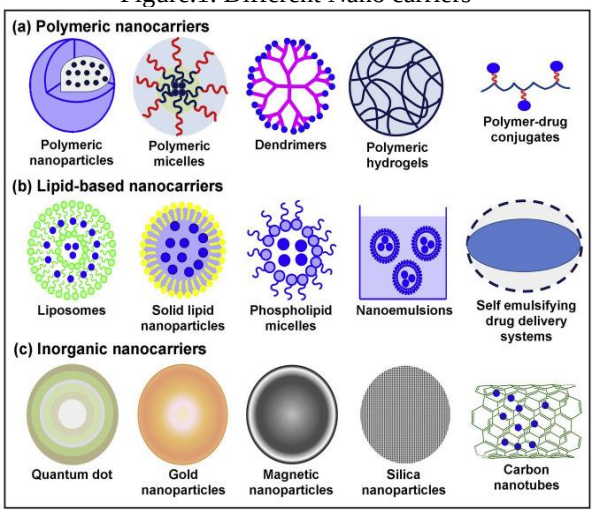

Fig.2 Solvent evaporation method

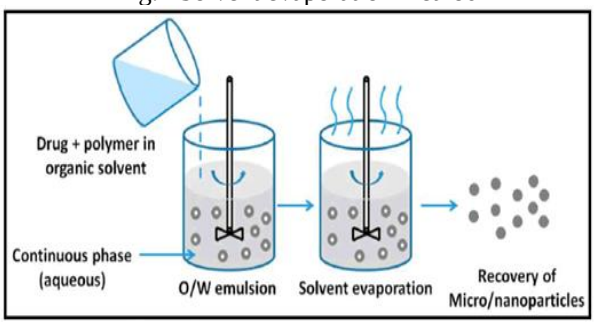

Fig.3. Nano-precipitation method

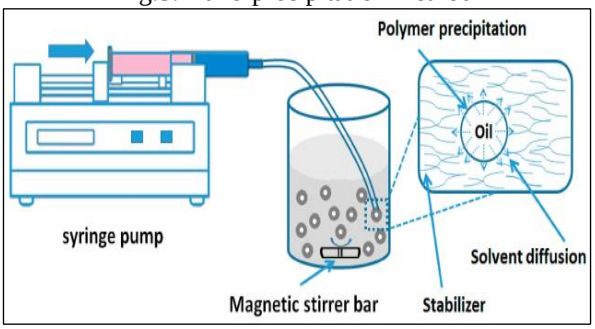

Fig.4 Emulsification/ solvent diffusion method

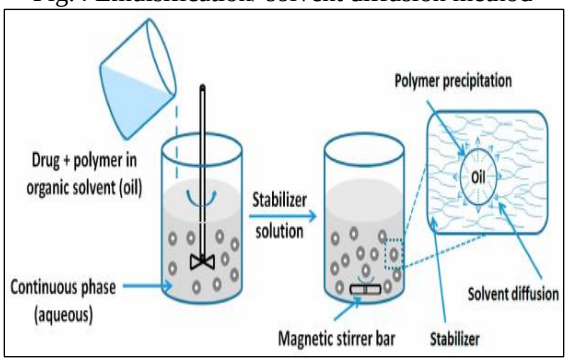

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Fig.5. methods for preparation of polymeric nano-particles

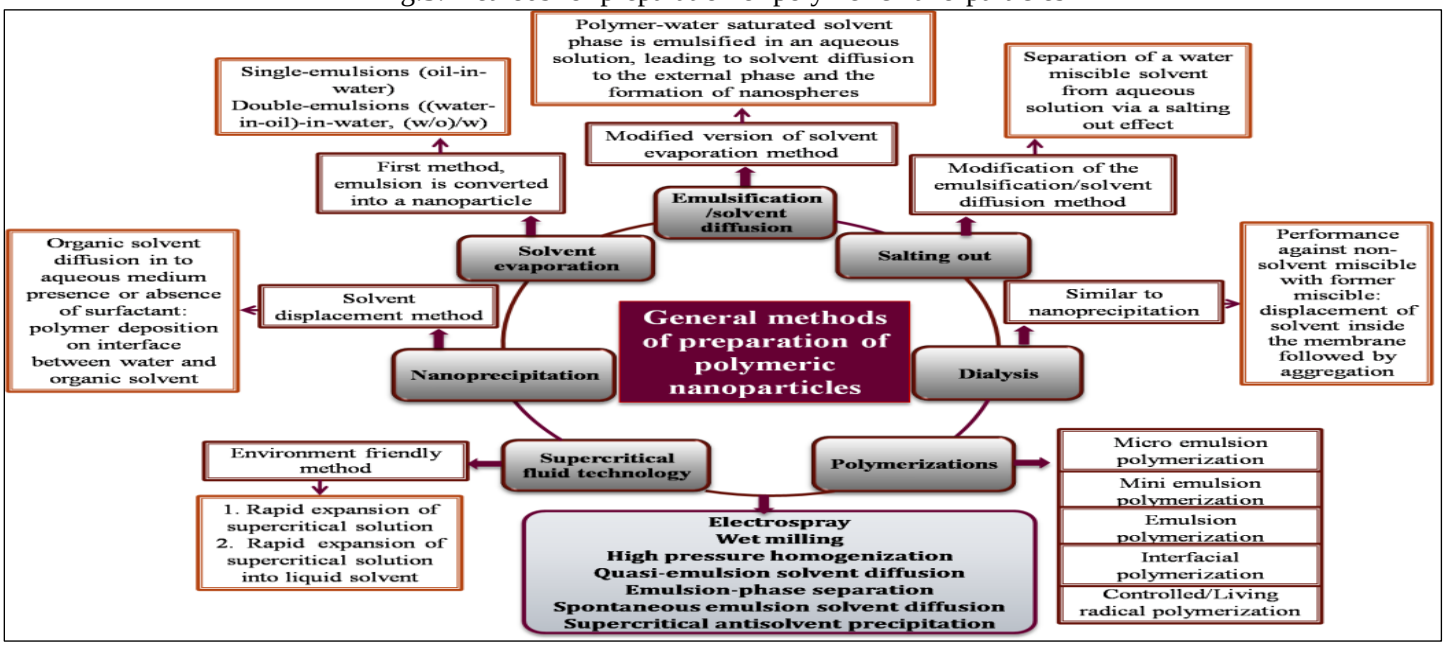

Table No. 2- Nano System and Properties

S.no	Types of Systems	Size (nm)	Characteristics	Applications
1.	Carbon nanotubes	0.5–3nm diameter and 20–1000nm Length	Third allotropic crystalline form of carbon sheets either single layer (single walled nanotube, SWNT) or multiple layer (multi-walled nanotube, MWNT). These crystals have remarkable strength and unique electrical properties.	Functionalization enhanced solubility, penetration to cell cytoplasm and to nucleus, as carrier for gene delivery, peptide delivery
2.	Dendrimer	<10nm	Highly branched, nearly monodisperse polymer system produced by controlled polymerization; three main parts: core, branch and surface.	Long circulatory, controlled delivery of bioactive, targeted delivery of bioactive to macrophages, Liver targeting.
3.	Liposome	50–100nm	Phospholipid vesicles, Biocompatible, versatile, good entrapment efficiency, offer easy surface functionalization.	Long circulatory, offer passive and active delivery of gene, protein, peptide and various other bioactive.
4.	Metallic nanoparticles	<100nm	Gold and silver colloids, very small size resulting in high surface area available for functionalization.	Drug and gene delivery, highly sensitive diagnostic assays, thermal ablation and Radiotherapy enhancement.
5.	Nanocrystals Quantum dots	2-9.5nm	Semi conducting material synthesized with II-VI and III-V column element; Size between 10 and 100 Å; Bright fluorescence, narrow emission, Broad UV excitation and high photo stability	Long term multiple color imaging of liver cell; DNA hybridization, immunoassay; receptor mediated endocytosis; labeling of breast cancer marker
6.	Polymeric micelles	10–100 nm	Block amphiphilic copolymer micelles, high drug entrapment, payload, biostability	Micelles 10–100 nm, blocks amphiphilic copolymer micelles, high drug entrapment, payload, biostability Long circulatory, target specific active and passive drug delivery, diagnostic value
7.	Polymeric Nanoparticles	10–1000nm	Biodegradable, biocompatible, offer complete drug protection	Excellent carrier for controlled and sustained delivery of drugs. Stealth and surface modified nanoparticles can be used for active and passive delivery of bioactive