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REVIEW ON VARIOUS APPROACHES ON PREPARATION, CHARACTERISATION AND APPLICATIONS OF POLYMERIC NANOPARTICLES

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ABSTRACT

Nanoparticles have evolved as a promising tool for the efficient delivery of drugs to alter and improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. The particle size of nanoparticle in the range of 10-1000nm. There has been a considerable research activities in the area of drug delivery using this nano particulate drug delivery system as carrier for many drugs, because of their targeted drug delivery system, controlled and sustained release properties, sub-cellular size, bio-adaptability, bio-compatibility with tissues and cells. The proper selection of polymers helps to design the drug release for specific location, increases the therapeutic effect and minimizes the side effects. In this review the various aspects of nanoparticle preparation, characterization, limitation, nanoparticle types, types of polymers, advantages-disadvantages and their applications were discussed.

KEYWORDS: Particle size, Zeta potential, Bioavailability, Targeted drug delivery.

INTRODUCTION

Polymeric nanoparticles are generally 10-1000nm in size.[1] These polymeric nanoparticles are prepared from the polymers, which have the nature of bio-comptability, bio-adaptability and bio-degradable. The drug is dissolved, entrapped, encapsulated to a nanoparticle matrix. The nanoparticles, nano-spheres or nano-capsules are obtained by depending up on the preparation. In nano-capsule system, the drug is confined to a cavity surrounded by uniform

polymer layer, while the nano-shell consists of matrix, in which the drug is physically and uniformly dispersed.[1]

In ordinary chemotherapy, the drugs are circulated non-specifically in the body. So they affect both diseased and healthy cells producing dose related side effects. These problems can be solved by using targeting of nanoparticles which includes increase in the drug concentration at the site of action and minimizing the toxic effects to the normal cells, such an advantage improves the drug safety also.

These carrier systems of nanoparticles effectively carry the drugs, proteins, DNA to the target cells and organs. And its nanometer size promotes effective permeation through the cell membranes and stability in the blood stream. The ability of choice of polymers helps to modify the carrier system of drug for desired properties.[1]

The hydrophilic polymers such as PEG is used for long circulating of nanoparticles for a prolonged time target to a specific organ as carriers of DNA in gene therapy and also their ability to deliver proteins, peptides and genes.[2]

The smaller sized particles have the large surface area due to this property of nanoparticles; the drug loading is relatively high and also increases the efficiency of drug.

The purpose of this review article is to summarize the ethics of nanoparticles such as limitation, advantage and disadvantage, preparation techniques of polymeric nanoparticles, types of polymers, types of nanoparticle used in the drug delivery system, characterization and application of nanoparticles.

Limitations Of Nanoparticles

The limitations of the nanoparticles are

1. The changes in physical properties make the particle-particle aggregation, difficult to handling of nanoparticles in liquid and dry forms due to smaller size and larger surface.[3]
2. The property of smaller particle sizes has the greater surface area makes the nanoparticles very reactive in the cellular environment.[3]
3. Due to the smaller particle size results in limited drug loading and burst release.[3]
4. It is essential to design the drug as enable to recognize the unique surface signature of their target cells.

5. The nature of the polymer should be compatible with body such as adaptability, biodegradable and biocompatible.

Advantages of Nanoparticles

- They control and sustain release of the drug during transportation and at the site of localization, alter organ distribution of the drug and regulate subsequent clearance of the drug so as to achieve increased therapeutic efficacy and reduced side effects.
- Surface engineering of the nanoparticles can be done to achieve both passive and active drug targeting after parenteral administration.
- Ability to incorporate hydrophilic and hydrophobic drug molecules
- By attaching targeting ligands to surface of nanoparticles, site specific targeting can be achieved.
- Prevent the multi-drug resistance mediated efflux of chemotherapeutic agents
- Nanoparticles can be delivered through various routes of administration including oral, nasal, parenteral, intra-ocular etc.
- Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
- Drug loading is relatively high and drugs can be incorporated into systems without any chemical reaction; this is an important factor for preserving the drug activity.
- Prolongs the half-life of the drug so that the frequency of administration can be decreased.
- Two- or more drugs can be delivered simultaneously for combination therapy to generate synergistic effect.

Preparation Techniques Of Polymeric Nanoparticles

Nanoparticles have been prepared most frequently by three methods: (1) dispersion of preformed polymers; (2) polymerization of monomers; and (3) ionic gelation or coacervation of hydrophilic polymers.

I.Preparation of nanoparticles from dispersion of preformed polymers

This technique can be used in various ways as described below

1. Solvent evaporation
2. Nanoprecipitation
3. Emulsification/solvent diffusion
4. Salting out

5. Dialysis
6. Supercritical fluid technology

II.Preparation of nanoparticles from polymerization of monomers

III. Preparation of nanoparticles by Ionic gelation/coacervation of hydrophillic polymers

IV. Preparation of nanoparticles by Solvent injection technique

Solvent Evaporation Method[1,2,3]

In this method, the polymer solution prepared by dissolving polymers is in an organic solvent (methylene chloride, chloroform or ethyl acetate for dissolving the hydrophobic drug). The mixture of polymer in organic solvent and drug solution in a suitable solvent is then emulsified in an aqueous solution of surfactant or emulsifying agent to make an oil in water (o/w) type of emulsion. Then the organic solvent is subjected to evaporation either by reducing the pressure or by continuous stirring. The particle size of the prepared nanoparticles are influenced by the type and concentrations of stabilizer, homogenizer/stiirer speed and polymer concentration. The high-speed homogenization or ultrasonication techniques are used to produce small particle size.

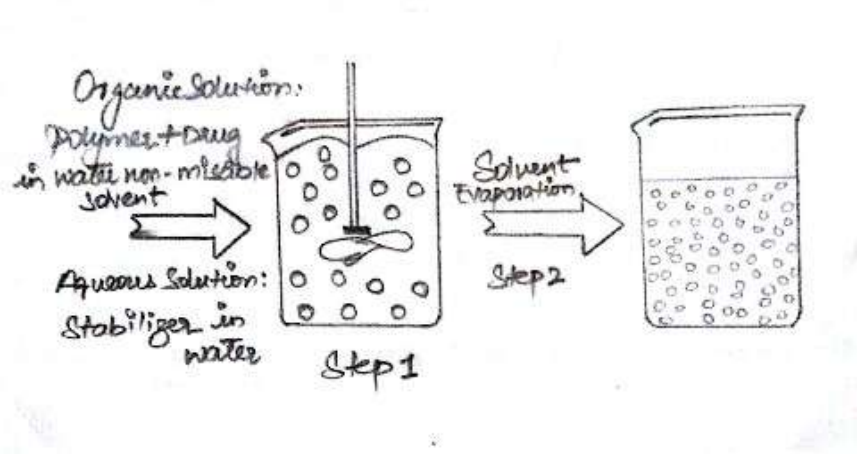

Fig.1..Solvent evaporation.

Nanoprecipitation[1,3]

The nano-precipitation or solvent displacement method involves precipiataion of polymer from organic solution. The organic solution contains preformed polymer and the diffusion of organic solvent in the aqueous medium in the presence or absence of the surfactant.In this method, the polymer is dissolved in a water-miscible solvent of intermediate polarity and added in to a aqueous solution containing a stabilizer as a surfactant with stirring. The

polymer deposition on the interface between the water and organic solvent due to rapid diffusion of the solvent which leads to the formation of colloidal nano suspension. The phase separation is achieved by the addition of totally miscible solvent but that is non-solvent of polymer.The nanoprecipitation is a widely used method for the preparation of polymeric or non-polymeric nanospheres because of its simplicity, rapidity, and reproducibility.

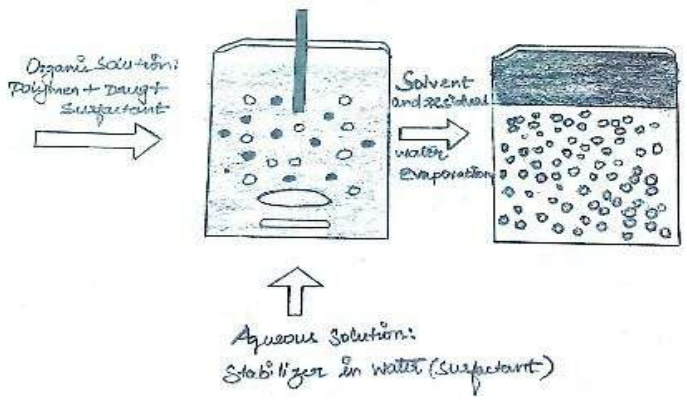

Fig.2.Nanoprecipitation.

Emulsification/Solvent Diffusion[1,3]

The solvent evaporation method is modified as emulsification/Solvent diffusion method. In this method, the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. As a result of spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leads to the formation of nanoparticles. As the concentration of water miscible solvent increases, a decrease in the particle size can be achieved. The solvent evaporation and solvent diffusion methods can be used for the preparation of nanoparticles for both hydrophobic or hydrophilic drugs. This technique is considered to be the ideal for the encapsulation of lipophilic drug.In the preparation of nanoparticles for hydrophilic drug, a multiple emulsion(w/o/w) needs to be prepared with the drug dissolved in the internal aqueous phase. The meso tetra (hydroxyl phenyl) porphyrin loaded poly (lactic-co-glycolic acid) nanoparticle, plasmid-DNA loaded PLA nanoparticles, coumarin loaded PLA nanoparticle, cyclosporine (CY-A) loaded sodium glycolate nanoparticle are the some of the examples that are prepared by using emulsification/solvent diffusion technique.

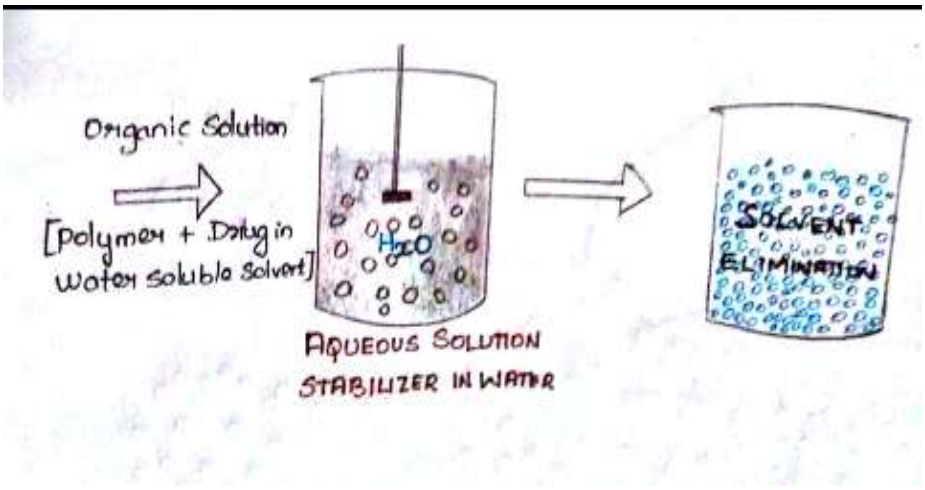

Fig.3.Emulsification/Solvent diffusion.

Salting Out[1]

Salting out is the method of separation of a water miscible solvent from aqueous solution through salting out effect. The procedure of salting out method can be considered as a modified method of the emulsification/solvent diffusion. The polymer and drug are first dissolved in a solvent such as acetone, which is emulsified into an aqueous gel containing the salting out agent such as electrolytes like magnesium chloride, magnesium acetate or non-electrolyte such as sucrose and also using colloidal stabilizer such as polyvinyl pyrolidine or hydroxyl ethyl cellulose. This emulsion of o/w is diluted with sufficient volume of water or aqueous solution to enhance the diffusion of acetone in aqueous phase, thus including the formation of nanospheres. The selection of salting out agent is important because it plays an important role in the encapsulation efficiency of the drug. Finally both the solvent and the salting out agent are eliminated by cross-flow filtration. So this technique is used in the preparation of PLA, poly (methacrylic) acid leads to high efficiency and also easily scaled up.

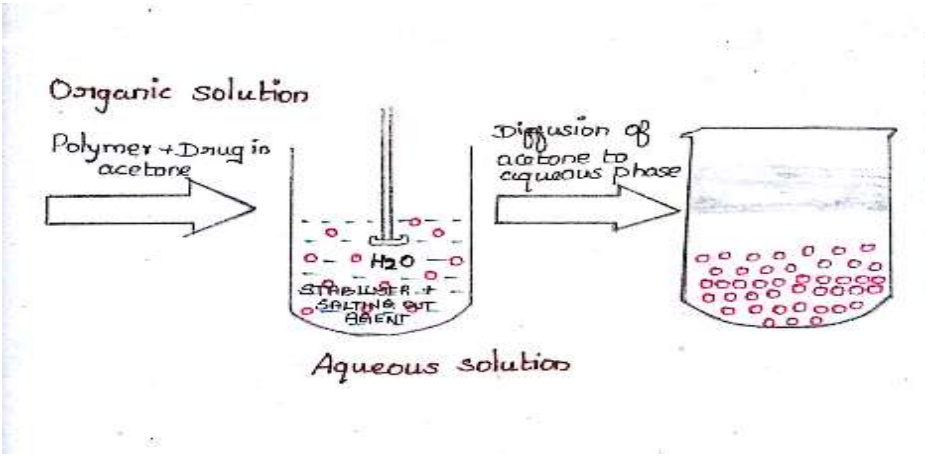

Fig.4.Salting out.

Dialysis[1]

The Preparation of nanoparticles by dialysis is very close to the nanoprecipitation method. The dialysis is based on a solvent displacement mechanism which includes, additional tools such as dialysis tubes or semi-permeable membranes with suitable molecular weight cutoff which serve as a physical barrier for the polymer . Thus, dialysis is performed against a nonsolvent of the polymer miscible with the polymer solvent. The displacement of the polymer solvent through the membrane induces a progressive loss of solubility of the polymer leading to the formation of homogeneous nano suspensions. The morphology and size of the particles can be affected by the nature of solvents used in the preparation of nanoparticles. The mechanism of polymeric nanoparticle formation by this method may be based on the similar mechanism of nanoprecipitation.

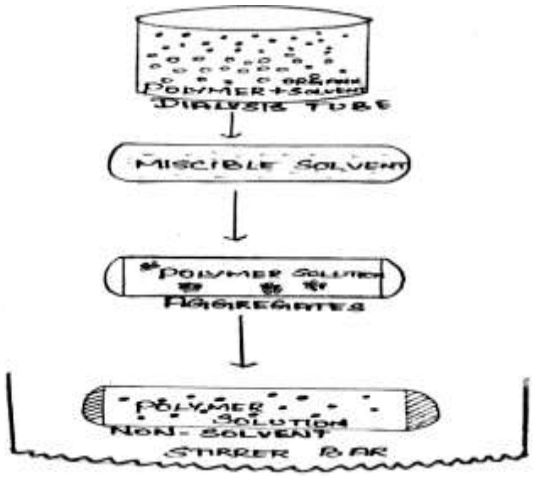

Fig.5.Dialysis.

Supercritical Fluid Technology[1,2,3]

The supercritical fluid technology is environmentally safer method for the production of polymeric nanoparticles. The utility of supercritical fluid has more environmental friendly solvents, and have the potential to produce polymeric nanoparticles with high purity and without any trace of organic solvent. Two procedures have been developed for the production of nanoparticles using supercritical fluid.

1. **Rapid expansion of supercritical solution.**
2. **Rapid expansion of supercritical solution into liquid solvent.**

Rapid Expansion of Supercritical Solution (RESS)

In this method, the solute is dissolved in a supercritical fluid to form solution, and then followed by the rapid expansion of the solution across the capillary nozzle into the ambient

air. The rapid pressure reduction in the expansion results the homogeneous nucleation and the formation of well dispersed particle. Generally, CO2 is the supercritical fluid used in the majority of studies. From the mechanistic studies resulting the solute have both nanometer and micrometer sized particles are present in the expansion jet. The degree of saturation and concentration of the polymer have a considerable effect on the size and morphology of the particle.

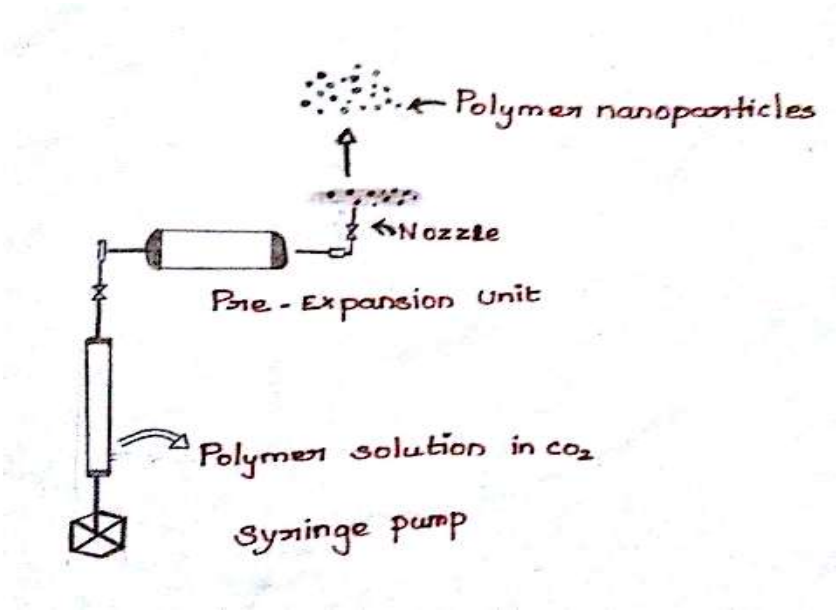

Fig.6.Rapid expansion of super critical solution(RESS).

Rapid expansion of supercritical solution in to liquid solvent

The procedure is almost similar to the above method but in contrary to the RESS, the expansion of the supercritical solution in to a liquid solvent instead of ambient air. The primary nanosized particles are not allowed to grow in the expansion jet due to the presence of the liquid solvent. For instance, poly(heptadecafluorodecylacrylate particles were produced using water as the solvent in which were expanded the supercritical solution and precipitated the polymer. It was shown that the particle formation results from the aggregation of initially formed nanoparticles. In addition, the presence of NaCl in the water phase helps to a better stabilization of the nanoparticles due to an increase in the ionic strength.

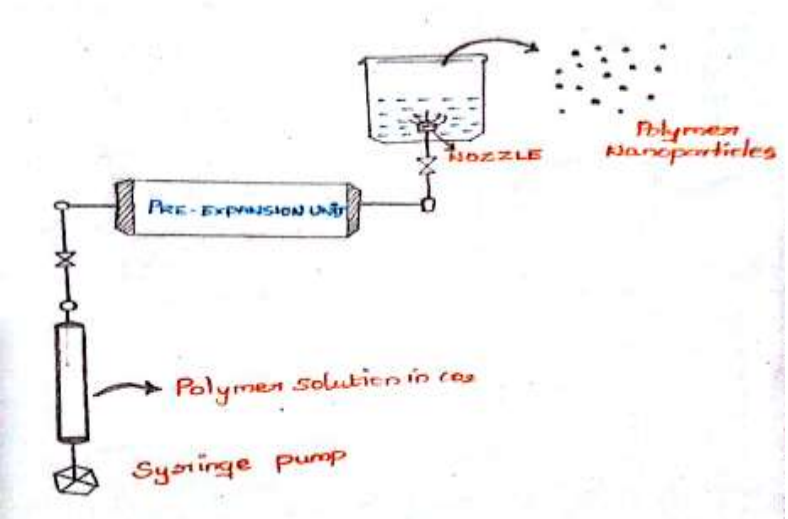

Fig.7.Rapid expansion of supercritical solution in to liquid solvent.

Preparation of nanoparticles by polymerization of monomer[1]

In this method, nanoparticles are prepred by polymerization of monomers. The nanoparticles are prepared either by dissolving polymerization medium or by adsorption of drug onto the nanoparticles after polymerization completed. The prepared nanoparticle suspension is purified by ultracentrifugation and re-suspending the particles in an isotonic surfactant-free medium to remove various ingredients such as stabilizers and surfactants employed for polymerization. The concentration of the surfactant and stabilizer used for the preparation of nanoparticles plays a significant role in the formation of nanoparticles and its particle size.

Ionic gelation technique/coacervation of hydrophillic polymers[1,2,3]

The biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate are used to prepare polymeric nanoparticles by ionic gelation method which was developed by cavlo and his co-workers. This method consists mixture of two aqueous phases, one is the polymer chitosan, di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO) and the other is a poly anion sodium tripolyposphate. The mechanism of formation of nanoparticles by this method is, positively charged amino group of chitosan interacts with negatively charged tripolyposphate to form coacervate with in its size range of nanometer. The coacervation of polymer and particles are formed by the electrostatic interaction between the two aqueous phases. In ionic gelation technique the material undergoing transition from liquid to gel due to the ionic interaction condition at room temperature

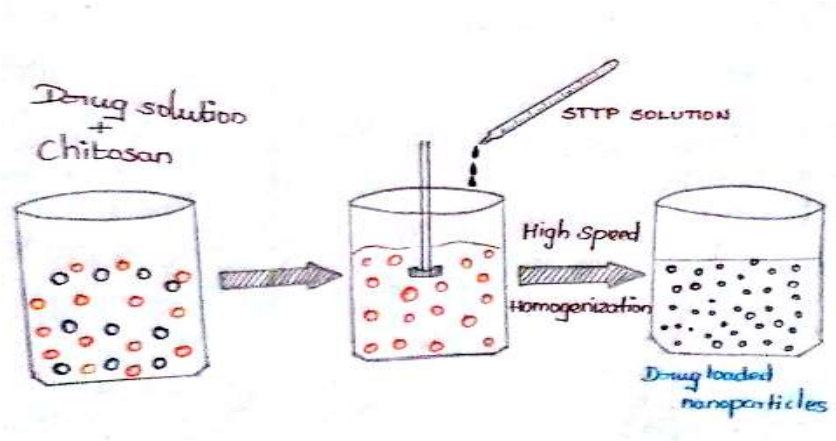

Fig.8.Ionic gelatin technique/coacervation of hydrophillic polymers.

Solvent Injection Technique[7]

Solvent injection technique is the novel approach of preparation of solid-lipid nanoparticles, The preparation of solid lipid nanoparticle by solvent injection technique is based the process of lipid precipitation from the dissolved lipid in solution. In this method, solid-lipid was dissolved in water miscible solvent such as ethanol, acetone and isopropyl alcohol. Then this solution of lipid was injected through the needle into aqueous phase containing surfactant with stirring .Then the solid lipid nanoparticle was filtered to remove any excess lipid. The incorporation of emulsifier in aqueous phase helps to the formation of lipid droplets at the site of injection and stabilizes the solid-lipid nanoparticle until the reduction of surface tension between water and solvent by solvent diffusion.

Types Of polymers used in nanoparitcle preparation

The polymers used for the preparation of nanoparticle should be biodegradable and biocompatible.They are classified as natural and synthetic (Table.1).

Table.1. polymers used in nanoparitcle preparation

Natural Polymers	Synthetic Polymers	Biodegradable Polymers	Non biodegradable Polymers
Chitosan Gelatin Sodium alginate Albumin	Polylactides (PLA) Polyglycosides (PGA) Poly (lactide co-glycolides) (PGA) Poly anhydrides Polyortho esters Poly cyanoacrylates Poly caprolactone Poly glutamic acid Poly malic acid Poly(N-vinyl pyrolidine)	Albumin Alginic acid/alginates Gelatin Chitosan and chitin derivatives Polylactic acid(PLA) Polyglycolic acid(PGA) Polylactide-co-glycolide(PLGA) Poly-e-caprolactone(PCL) Polylactide-co-caprolactone(PLC) Polyalkyl cyanoacrylates	Polymethyl vinyl ether/maleic anhydride Gantrez Polymethyl methacrylates (Eudragit) Polyamidoamines. (PAMAM)

	Poly(methyl methacrylate) Poly (vinyl alcohol) Poly (acrylic acid) Poly acrylamide		

Types of nanoparticle used in drug delivery system[6]

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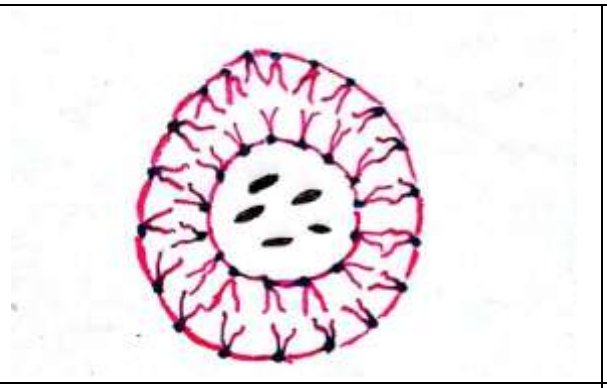
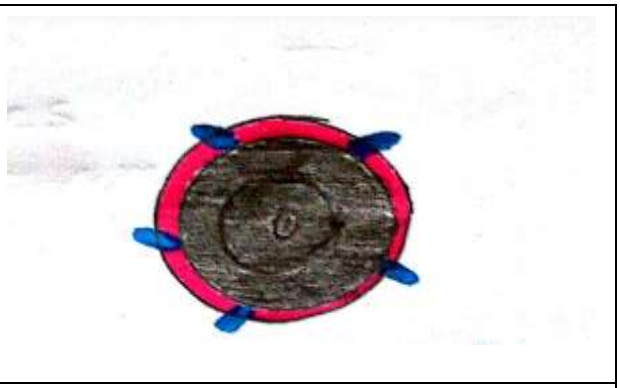
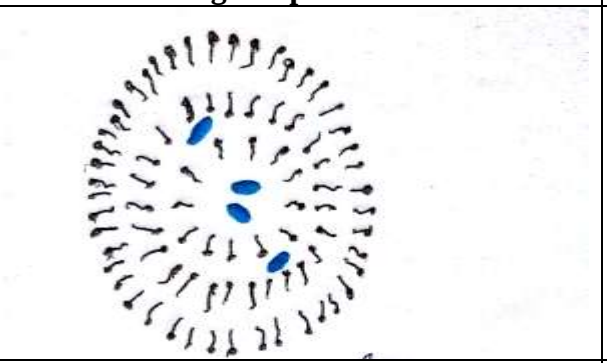
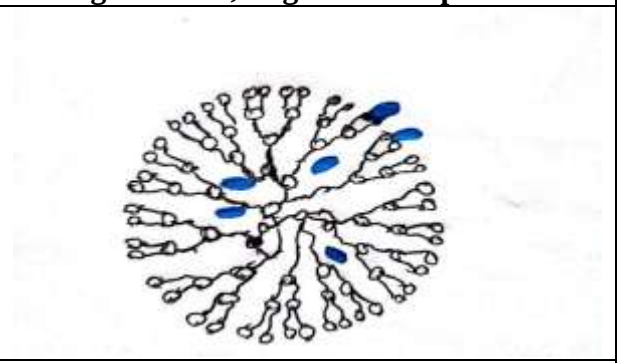
<tr><td>  </td><td>  </td></tr>
<tr><td>Fig.9.Liposomes</td><td>Fig.10.Silica;magnetic nanoparticle.</td></tr>
<tr><td>  </td><td>  </td></tr>
<tr><td>Fig.11.Solid-lipid nanoparticle.</td><td>Fig.12.Dentrimers.</td></tr>
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Characterization of nanoparticles

Generally the nanoparticles are characterized by their size, morphology and surface charge by using advanced technique such as scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM).[3] The physical stability and the *invivo* distribution of the nanoparticles are affected by particle diameter, size distribution and charge of the particle. The discovery of electron microscope is very useful to determine the overall shape of the polymeric nanoparticle. The charge on the surface of the nanoparticles affects the physical stability and dispersion of the polymer as well as their *invivo* performance.[3]

Particle Size[2,3]

The morphology and size of the particle are the most important parameters for the characterization of nanoparticles. The electron microscope is used for the measurement of

particle size. The particle size affects drug release. The smaller particles offers large surface area as the result shows high therapeutic efficiency. The major drawback of smaller particle size offers the aggregation during storage, so it needs maximum stability. The degradation of polymer also affects the particle size. There are several methods for determining nanoparticle size which are given below.

1. Dynamic scattering light/photon correlation spectroscopy.
2. Scanning electron microscopy.
3. Transmission electron microscope.
4. Atomic force microscopy.

Surface charge of nanoparticle[2,3]

The surface charge of the nanoparticle is very important to determine their biological interaction as well as electrostatic interaction with bioactive compounds. When the nanoparticles administered intravenously, the body immune system (IgG) recognize and cleared by phagocytes from the circulation. Apart from the fate of size and its surface hydrophobicity also determines the adsorbed components in blood, mainly proteins (opsonins).

After the success of drug targeting by nanoparticle, it is necessary to minimize the opsonization and prolong the circulation.This can be overcome by using hydrophilic polymers/surfactants for coating on the surface of the nanoparticle.

Using biodegradable co-polymers such as polyethylene glycol (PEG), polyethylene oxide, poloxamine, polyoxamer and polysorbate 80 (tween 80).

The surface charge property is characterized by zeta potential of the nanoparticle. The stable suspension nanoparticles with zeta potential are above (+/-) 30mV. The zeta potential ensures stability, avoid aggregation of the particle and used to determine whether the encapsulation of charged active material is with in the centre of nanocapsule or coated on the surface.

Surface Hydrophobicity[3]

The surface hydrophobicity determines the amount of adsorbed blood components, mainly opsonins (proteins). These surface hydrophobicity influences the binding of opsonins on the nanoparticle surface called opsonization. It acts as a bridge between nanoparticles and phagocytes. The technique to determine the surface hydrophobicity are hydrophobic

interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc.

The x-ray photon correlation spectroscopy permits the detection of specific chemical groups on the surface of nanoparticles.

Drug Loading[2,3]

The loading of drug in nanoparticulate system can be done by two methods. They are given below.

- **Incorporation method**

Incorporating at the time of nanoparticle production.

- **Adsorption/absorption technique**

Absorbing the drug after the formation of nanoparticles by incubating the carriers with a concentrated drug solution.

The drug loading and entrapment efficiency on the solid-state drug solubility in matrix material or solid dissolution or dispersion of polymer, which is related to the composition of polymer such as molecular weight, the drug-polymer interaction and the presence of the end functional groups (ester or carboxyl).

Drug content

Drug content in nanoparticles must be determined by adequate analytical method which measures both the freeze drying concentration as well as entrapped drug concentration using high and its value. It is compared to before freeze drying to detect any leakage of drug from nanoparticles.

The total drug content was calculated as follows

$$\text{Total Drug Content} = \frac{\text{Volume total}}{\text{Volume aliquot}} \times \text{drug amount in aliquot}$$

Entrapment efficiency was calculated as follows:

$$DEE\% = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \times 100$$

Crystalline Status[5]

The crystalline status are determined by different analytical methods such as differential scanning calorimetric, x ray diffraction and other methods are used to determine any possible changes such as physical form, amorphous or crystalline structure and other polymeric changes in the formulation of drug. At present x ray diffractometer are used to determine the different polymorphs.

Toxicity Evaluation[5]

The some important acute toxicity is associated with nanosystem. They are inflammation and granuloma formation due the enhancement of endocytosis system; the generation of free radical causes cell death by the oxidative stress and altered/modified protein/gene structure resulting in immune system. The long term toxicities are bioaccumulation, poor biodistribution and ultimate fate of nanosystem in the body.

Thermal analysis by differential scanning calorimeter[5]

During storage freeze dried nano particles included with in a vitrified matric of lyo-protectant which must be stirred at temperature below the temperature of glass transition, to prevent any shrinkage of freeze dried cake. The temperature may be determined by differential scanning colorimetry. This technique is very useful to study the interaction between the lyo-protectants and nanoparticles.

Drug Release[2,3]

The main reason for pursuing nanotechnologies is to deliver drugs. Hence the releasing of drug molecule is very important. The drug is released by the separating of drug and the carrier molecule. So both the drug activity and polymer biodegradation are the important factors. Generally, the drug release depends on the factors such as.

- Solubility of drug.
- Desorption of the surface bound/adsorbed drug.
- Drug diffusion through the nanoparticle matrix.
- Nanoparticle matrix erosion/degradation.
- Combination of erosion/diffusion process.

Evaluation Methods For Release Of Drug[2,3]

The various methods are use to study the invitro release of the drug from nanoparticles are

- Side by side diffusion of cells with artificial or biological membrane.

- Dialysis bag diffusion technique.
- Reverse dialysis bag technique
- Agitation followed by ultracentrifugation/centrifugation.
- Ultra-filtration or centrifugal ultra-filtration techniques.

Application Of Nanoparticles

- Targeted drug delivery system
- Long circulating nanoparticles
- Reversion of multi-drug resistance in tumor cells
- Nanoparticles for oral delivery of peptides and proteins
- Nanoparticles for drug delivery into brain.
- Targeting of nanoparticles in the GI tract using ligands
- Nanoparticles for respiratory tract
- For diagnosis and bio-imaging
- Tissue repair
- Ophthalmic administration

Targeted Drug Delivery System[2,3]

The diseased tissues are specifically targeted by nanoparticles with appropriate size, selective binding, reduced non-specific toxicity and enhance the delivery of drugs.Timed release of drug and it must remain encapsulated until reaching of targeted site.It will able to deliver a concentrate dose of drug in the near of the tumor target with short period of time and enhanced the permeability, and will reduce the drug exposure on the healthy tissues.

Long Circulating Nanoparticles[2]

The hydrophilic polymers such as polyethylene glycol, poloxamines, poloxamines, poloxamers and poly saccharides are used for the coating of nanoparticles. These hydrophilic polymers are invisible to the macrophages or phagocytes, because of its dynamic cloud of hydrophilic and neutral chains at the surface of particle repels the plasma protein. So it remained in the circulation for a longer period of time.

Reversion of multidrug resistance in tumor cells[2]

The anticancer drug produce limited efficacy against tumor cells, because the cancer cells are able to develop the resistance against the drug. The resistance mechanism allows tumor to evade chemotherapy. The multidrug resistance occurs mainly due to the over expression of p-

glycoprotein in the plasma membrane, by reaching the drug. The overcome of tumor cells resistance is replaced by bypassing the anticancer drug with the help of using colloidal carriers via p-glycoprotein mediated multidrug resistance.

If once the drug crosses the plasma membrane, the p-glycoprotein does not recognize the drug to effluxes out. So the colloidal carriers of nanoparticle play a major role in the multidrug resistance of tumor cells.

Nanoparticles for oral delivery of peptides and proteins[2,3]

The bioavailability of these molecules is limited due to the presence of epithelial barriers in GIT. So encapsulation of polymeric nanoparticles protects them against hydrolytic and enzymatic degradation.The GIT provides various physiological and morphological barriers against the delivery of proteins and peptides. They are

- Proteolytic enzymes in the gut such as pepsin, trypsin, chymotrypsin.
- Endopeptidase at brush border membrane.
- Bacterial gut flora.
- Mucus layer and epithelial cells.

Thus overcome by these types of GIT barriers with the help of colloidal carriers system.

Targeting of nanoparticles in the git using ligands[2]

The enterocytes and M cells (micro fold cells) of payer's patch in the GIT shows cell specific carbohydrates which may serve as binding site to the colloidal drug carriers with suitable ligands. To improve the interaction of nanoparticles with M cells of payer's patches and adsorptive enterocytes by utilizing specific binding ligands or receptor based upon the non-specific adsorptive mechanism.

Nanoparticles for gene delivery[2,3]

This system facilitates bone healing by using poly (lactic-co-glycolic acid) polymers containing therapeutic genes such as bone morphogenic protein.

Nanoparticles for drug delivery into brain[2,3]

The polysorbate 80/LDL, transferrin receptor binding antibody such as OX26, lactoferrin, melano transferring and cell penetrating peptides having a capable of delivery the self non-transportable drug into the brain. It has been reported to the delivery of hexapeptide dalargin, doxorubicin and other agents into the brain by using of poly (butyl cyanoacrylate), which is

significant because of the greater difficulty for drugs to cross the blood brain barrier. In spite of these some reported success with polysorbate 80 coated nanoparticles and including desorption of polysorbate coating, rapid nanoparticle degradation and toxicity caused by using of high concentration of polysorbate 80.Then OX26 monoclonal antibodies (anti-transferrin receptor monoclonal antibodies) is the most studied blood brain barrier targeting antibody has been used to enhance the penetration of liposome's. The brain uptake of lactoferrin, an iron-binding glycoprotein (transferrin family) is twice that of OX26 and transferrin invivo was recently demonstrated.

Nanoparticles for respiratory tract[3]

The application of nanoparticles on respiratory tract avoids the normal phagocytic defenses in respiratory tract and improves the systemic circulation and may reach to CNS. In the treatment of respiratory disease, aerosol therapy is the most convenient method for the delivery of drug into the lungs.Due to this aerosol therapy, bioavailability of the drug should not affected because of the avoidance of first pass metabolism and direct delivery to the site of action and also lungs having the availability of huge surface area for local and systemic absorption of drug.The colloidal carriers (nanocarrier system) is used for drug delivery in the aerosol form and it offers many advantages such as uniform distribution of the drug dose among the alveoli, improved solubility of the drug from its own aqueous solubility, improves the patient compliance sustained release and reduce the side effects.

For diagnosis and bioimaging[3,8]

The available of molecular imaging techniques such as optimal imaging (OI), magnetic resonance imaging (MRI), ultrasound imaging (USI), positron emission tomography (PET) and others also having reported for imaging of *invitro* and *invivo* biological specimens.

The technique of luminescent and magnetic nanoparticles are advancely developed bio-imaging technologies. There are two different types of nanoparticles have been widely used for imaging such as luminescent nanoprobes for optical imaging and magnetic nanoparticles for magnetic resonance imaging.

The micro-chips produced successfully by the nano-biotech scientists that are coated with human molecules, where the molecule detects the sign of disease. The designed chip emits the electrical impulse signal.

The nanobot are the special sensor can be inserted into the body under the skin and it warns of any possible disease by its own checking of blood contents. It can also used to monitor the sugar level in blood. Gold nanoparticles are used to detect cancer by using ultra-sensitive fluorescent probe for detection.The magnetic nanoparticle used in the biomedical application such as cellular labeling/cell separation detoxification of biological fluid and magnetic resonance imaging.

Tissue repair[3]

The damaged tissue is repaired by using iron-oxide nanoparticle through the opposing of two tissue surfaces then heating the tissues sufficiently to join by soldering.The protein or synthetic polymer coated nanoparticle are placed between the surface of tissues enhance the joining of tissues. Then the temperature fifty degrees Celsius or greater are known to induce by the denaturation of protein and the subsequent entanglement of adjacent protein chain.The nanoparticles absorbs the light strongly from the laser are also useful for tissue repairing procedures. So designed specifically gold or silver coated iron-oxide nanoparticles are strongly absorbs the light. This technique provides minimization tissue damaging by using the least harmful wavelengths of lights or lower powered light sources.

CONCLUSION

The review was to describe about the preparation techniques, limitation, types of polymers, and types of nanoparticles, advantages and evaluation of nanoparticles. A significant progress has been made toward achieving nanoparticulate drug delivery system that can effectively treat diseases. Various nano particulate technologies are researched and brought in the market, which surely assure a bright and promising future. Hence it can be concl;uded that the nanoparticulate drug delivery technology is considered to an ideal drug delivery system to deliver the drug substances such as genes, enzymes, poor soluble drugs, poorly absorbed drugs and labile biologically active substances.

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