Recent Advances in Nanoparticle-Based Drug Delivery Systems: A Review

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ABSTRACT

Nanoparticle-based drug delivery system offering controlled, targeted and efficient drug delivery and emerged as a promising strategy for cancer therapy. The unique physical and chemical properties like, high surface area, adjustable size and enhanced permeability, enable precise tumour targeting through active, passive and stimuli-responsive mechanisms.

There are various nanocarriers such as liposomes, polymeric nanoparticles, dendrimers and metallic nanoparticles have been explored for gene therapy , immunotherapy and chemo therapy.Nanoparticles are particulate dispersions or solid particles with a size in the range of 10-1000nm and the drug is dissolved, entrapped, encapsulated or attached to nanoparticle matrix. Nanoparticles offers an significant advancement in the delivery of drug, addressing fundamental challenges. The use of nanoparticles in tissue engineering , medication (drugs) transport, imaging, sensing, disease diagnostics, and treatment holds great promise for understanding fundamental biological processes. To achieve efficient drug delivery it is most important to understand the interactions between nanomaterials with the biological environment, targeting cell surface receptors, drug release, combination drug administration and stability of therapeutic agents.

Key Word: Nanoparticles, Liposomes, Niosomes, Mechanism.

INTRODUCTION [1,2,3,4]

Nanoparticles are defined as a particulate dispersion or solid particles with a size of 10-1000nm. Firstly the drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix, depending on the method of preparation, nanospheres, nanospheres, or nanoparticles can be obtained. Nanoparticles refers to a large number of family of materials like organic and inorganic. Each materials have their unique and tunable properties and can selectively designed for specific applications. The primary goals of the formulation of drugs into the nanocrystals is the increase in particle surface area in contact with the dissolution medium, therefore increasing bioavailability.

Nanoparticles are the system in which the drug is enclosed to a cavity surrounded by unique polymers membrane, while the nanospheres are matrix systems where the drug is physically and uniformly dispersed. In recent year, the biodegradable polymeric nanoparticles are coated with hydrophilic polymers such as polyethylene glycol(PEG), have been used as potential drug delivery devices because of their ability to circulate for the prolonged or extended period time to target a particular organs, as a carrier of DNA in gene therapy.

ADVANTAGES [4,5]

- Controlled release of drug over the prolong or extended period of time.
- Protection of encapsulated drug against chemical degradation.
- Feasibility of incorporation of both hydrophobic and hydrophilic.
- Enhancement of solubility and bioavailability of the drugs.
- Useful for the targeted and controlled drug delivery.
- Decreased the toxicity or side effects of the drugs.
- Release the drug on the site of action.
- Biodegradable material or polymers.

- Have longer shelf-life
- Does not cause any toxicity.
- Higher carrier capacity.
- Early disease detection.

DISADVANTAGES [4,5]

- Elimination and metabolism of drugs vary with different types of materials used in the nanoparticles synthesis.
- Due to moderate loading capacity could crystallize after prolonged storage conditions.
- Non-degradable polymers used in drugs tend to accumulate in tissue.
- Unpredictable genotoxicity due to insufficient toxicological assessment studies.
- High cost of synthesis materials.
- Poor dispersion abilities.

TYPES OF NANOPARTICLES [3,6]

There are the following types of nanoparticles are listed below.

- Solid lipid nanoparticles (SLNs)
- Nanostructured lipid carriers (NLC)
- Super paramagnetic nanoparticles
- Quantum dots
- Liposomes
- Fullerenes
- Nanoshells

- **Solid lipid nanoparticles (SLNs)**

Solid lipid nanoparticles are mainly comprise lipids that are in solid phase at room temperature and ranging from 50-1000nm.which are composed of lipid dispersed in water or aqueous surfactant solution. SLNs offers an unique properties such as small size, larger surface area and high drug loading.

Many methods are used for preparing SLNs include high pressure homogenization (hot or cold), ultrasonication homogenization, solvent evaporation, etc.

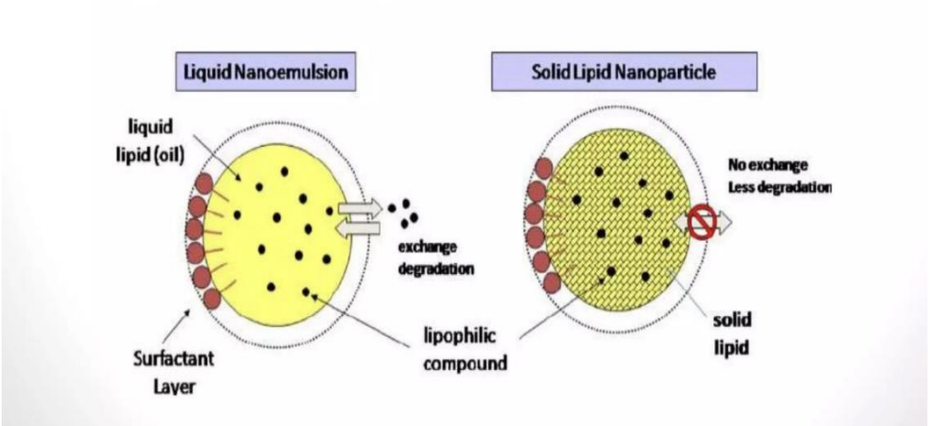


Figure:1- Solid lipid nanoparticles

- **Nanostructured lipid carriers (NLC)**

Nanostructured lipid carriers are produced by the blend of solid and liquid lipids. In lipid-based nanosystem is introduced as biocompatible, non-toxic and safe nano drug delivery systems. NLCs can be used to treat a variety of diseases such as hypertension, cancer, infections, diabetes and pain management. Drug release from lipid particles can occurs by the diffusion and simultaneously by the lipid degradation in the body.

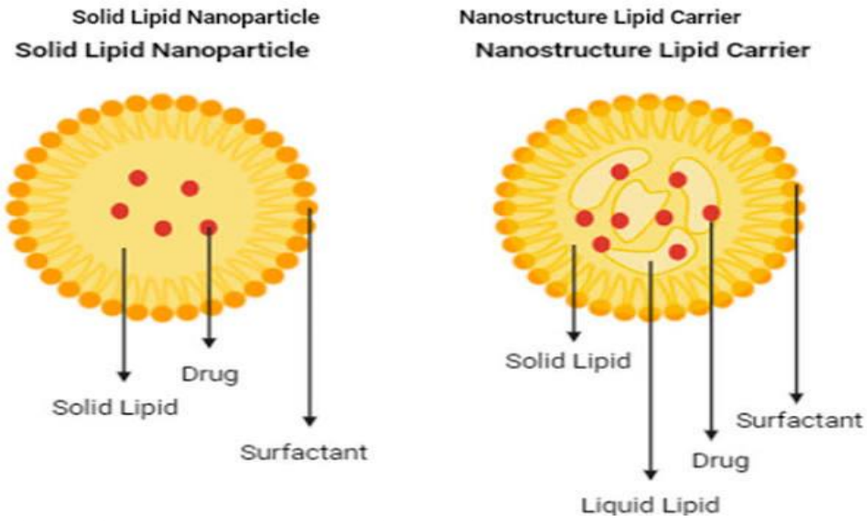


Figure:2- Nanostructured lipid carriers

- **Super paramagnetic nanoparticles**

Super paramagnetic nanoparticles are those molecules which are attached to a magnetic field. Nanoparticles of iron oxide with diameter in the range 5-10 nm have been used for the selective bioseparations . It involves the technique coating the particles with an antibodies to cell-specific antigens, used for the separation from the surrounding matrix. The magnetic nanoparticles that magnetize in an external magnetic field but loose their magnetism when the magnetic field is removed.

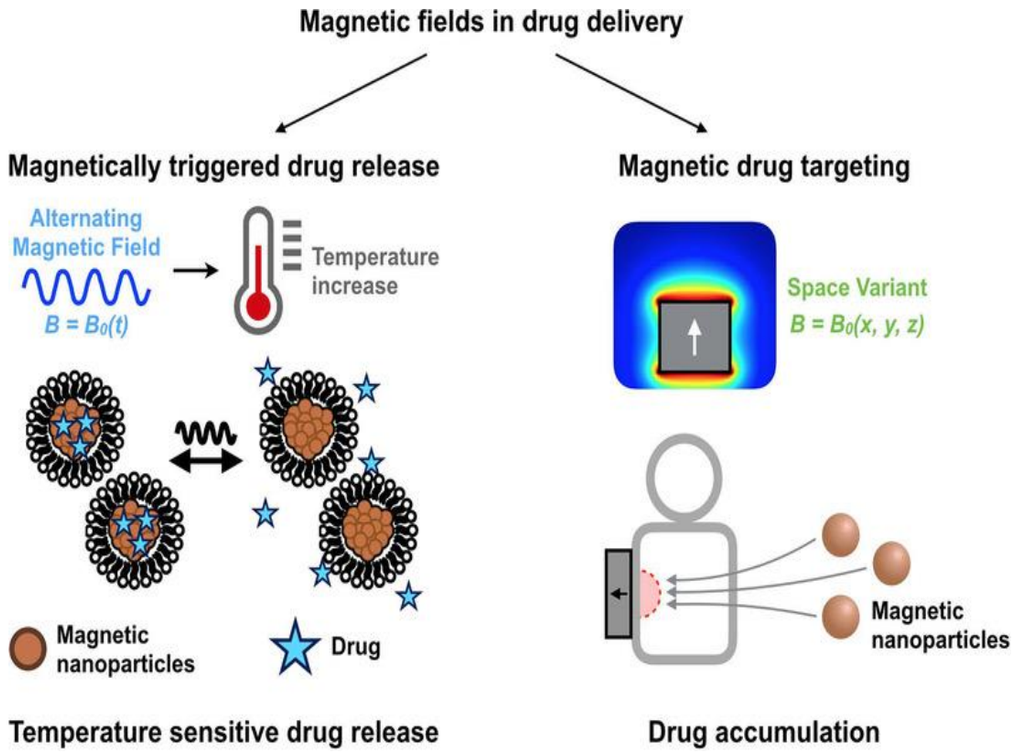


Figure:3- Super paramagnetic nanoparticles

- **Liposomes**

Liposomes are small vesicles or vesicular structures with an aqueous core surrounded by a hydrophobic lipid bilayer, created by the ejection of phospholipids. It is used in the various tissue engineering applications because the manufacturing materials of liposomes and cell membrane are similar. Liposomes can vary in size, range from 15 nm to several 1m and have a single layer (unilamellar) or have multiple bilayer (multilamellar) structures.

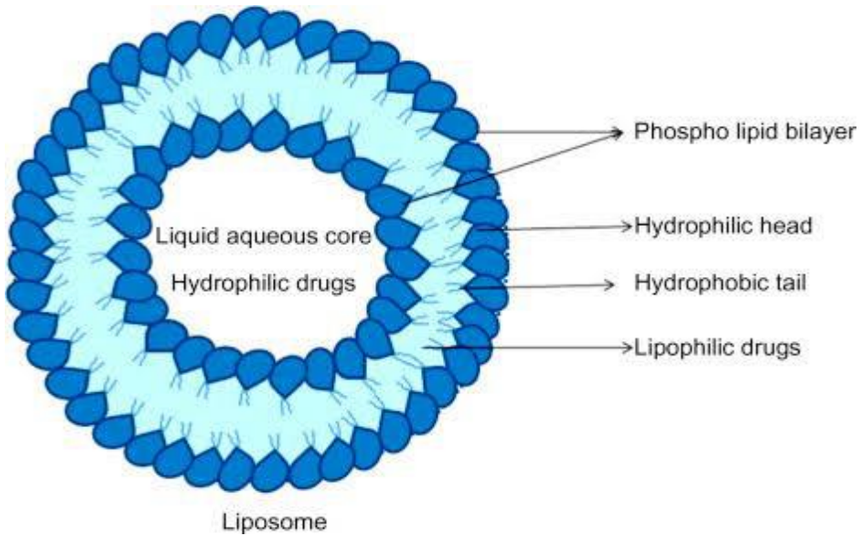


Figure:4- Liposomes

- **Fullerenes**

Fullerenes is any molecule which is entirely composed of carbon, in the form of hollow sphere, ellipsoid, or tube. Fullerenes are used for several biomedical applications including the design of standard-performance MRI contrast agents, X-ray contrast agents, photodynamic therapy and drug and gene delivery.

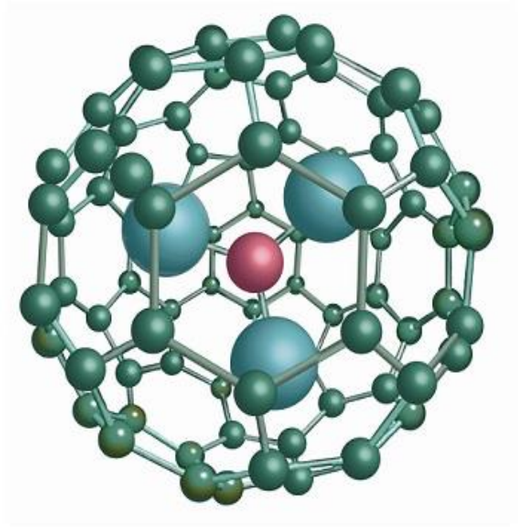


Figure:5- Fullerenes

- **Nanoshells**

Nanoshells are spherical cores of a particular compound surrounded by a shell or outer coating of thin layer of an other materials, which is a few 1-20 nm thick. Nanoshells involves quasiparticles called a plasmon that is a collective excitation or quantum plasma oscillation where an electrons simultaneously oscillates with respect to all the ions.

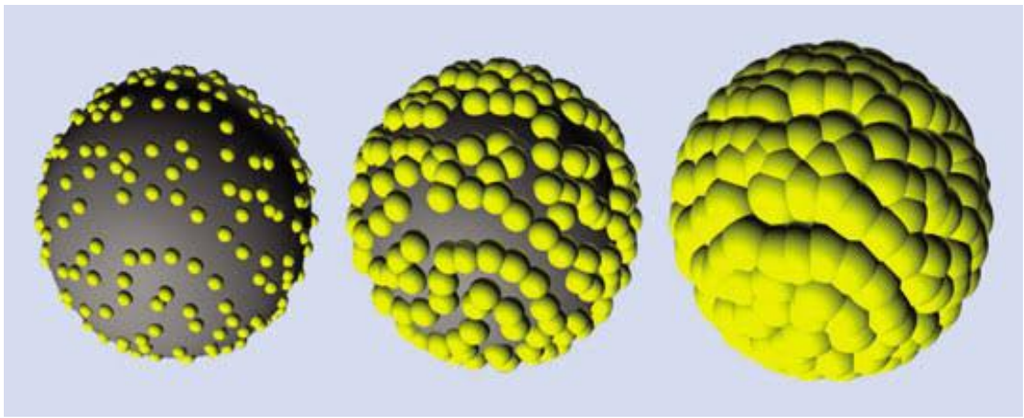


Figure:6- Nanoshells

- **Quantum dots**

Quantum dots are the semiconductor nanocrystals and core shell nanocrystals which contains the interface between different semiconductor materials. The size of quantum dots from 5-20 nm in diameter and the particles which are smaller than 5nm are quickly cleared from the renal filtration. The quantum dots acts as an artificial atom, whose properties can be controlled.

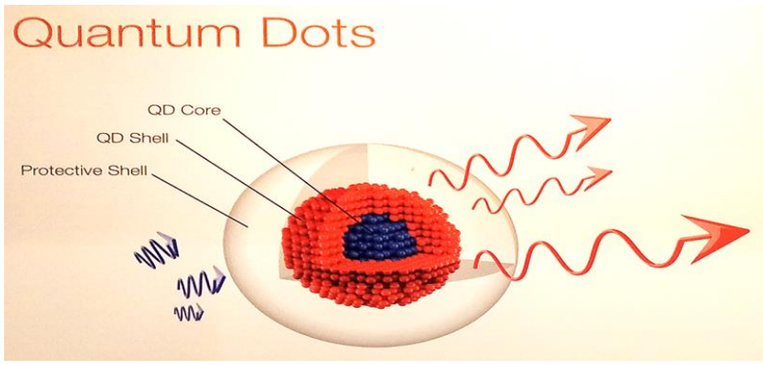


Figure:7- Quantum dots

METHOD OF PREPARATION [7,8]

There are the various methods used for the preparation of nanoparticles as follows-

- Emulsion Polymerization
- Desolvation Method
- High Pressure Homogenization
- Control Gellification Method
- Controlled Nanoprecipitation without Surfactants
- Solvent Evaporation Method
- Solvent Diffusion Method
- Supercritical Fluid Extraction
- Melt Emulsification and Homogenization Method

Emulsion Polymerization

It is a method in which the monomer to be polymerized is emulsified in non-solvent phase.There are two method used for the emulsion polymerization process.

1) Micellar nucleation and polymerization
2) Homogeneous nucleation and polymerization

1)Micellar nucleation and polymerization

- In this method monomer is emulsified in non-solvent phase using surfactant molecules.
- This leads to formation of a monomers-swollen micelle and stabilized monomer droplets.
- The polymerization reaction yield through nucleation and propagation.

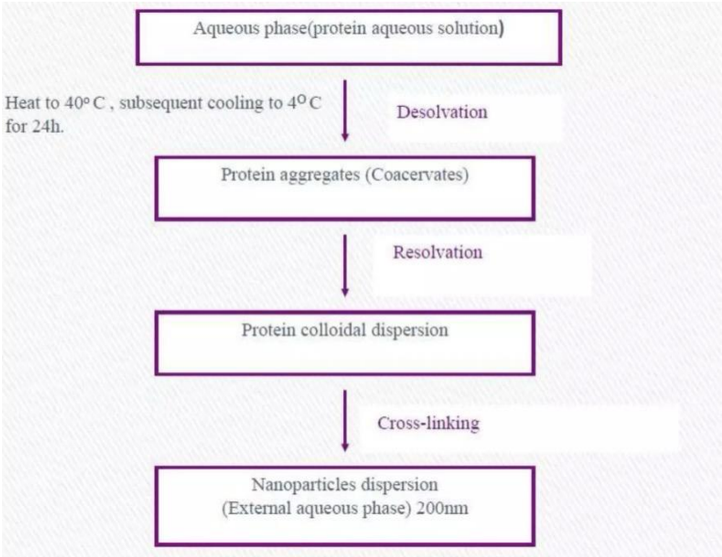
2)Homogeneous nucleation and polymerization

- In this method monomer is soluble in continuous outer phase and both nucleation and polymerization can directly occur in this phase leads to the formation of primary chains called oligomers.
- When the oligomers reach certain length, they precipitate and form primary particles and stabilizes by the surfactant molecules in which the drug will be entrapped to form nanoparticles.

Desolvation Method

Polysaccharides or proteins from an aqueous phase can be desolvated by:

- pH change
- Change in temperature
- Addition of an appropriate counter ion.
  (e.g. alginate).



High Pressure Homogenization

It is a technique which uses high pressure (upto thousands bars) to force a liquids via a narrow gaps by creating intense shear, cavitation, and impact forces that break down the particles and droplets on nanoscale. It produces stable nanoemulsions, nanocrystals,lipid nanoparticles and polymeric nanoparticles.

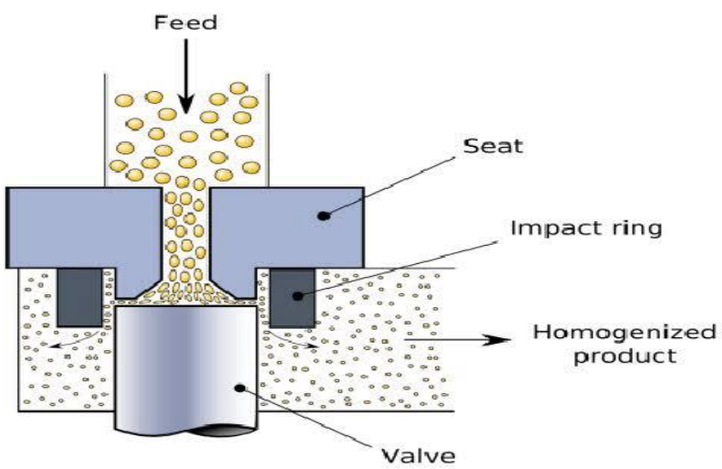
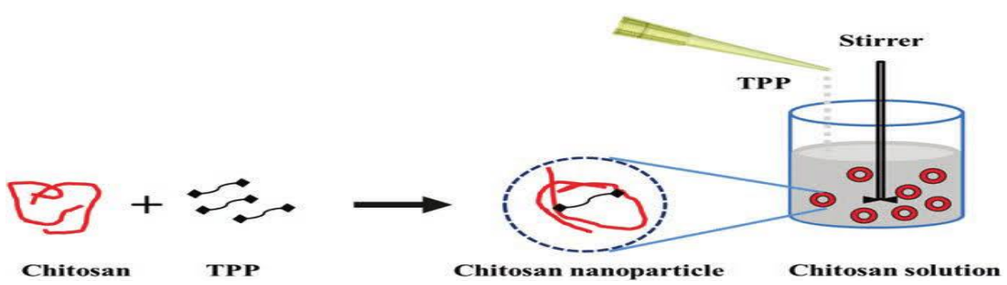


Figure:8- High pressure homogenizer

Controlled Gellification Method

Controlled gellification is also known as ionic gelation method. It involves the creating an nanostructures by electrostatic interaction between charged polymers(chitosan) and oppositely charged cross-linkers. This method is highly efficient for producing spherical and biocompatible nanoparticles (200-1000 nm).

Figure:9- Controlled gellification method



Controlled Nanoprecipitation without Surfactants

- This method is based on interfacial deposition of polymer by displacement of a semi polar solvent miscible with water(aqueous) from a lipophilic solution.
- An organic solvent is diffuses to the external aqueous phase induces the immediate precipitation of polymers because of the complete miscibility of both phases.
- If the drug is highly hydrophilic it diffuses out into an external aqueous phase while if the drug is hydrophobic it precipitates in aqueous phase as nanocrystals.

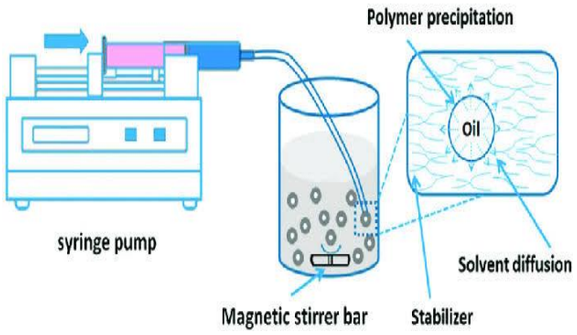


Figure:10- Nanoprecipitation Method

Solvent Evaporation Method

- Solvent evaporation method involves the formation of conventional O/W(oil in water) emulsion between partial water miscible solvent.

  e.g.PLGA nanospheres

- Polymer is solubilized in (chloroform) solvent and spread in gelatin solution by sonication process to yield O/W(oil in water) emulsion. The solvent is removed by evaporation and homogenizer are used that breaks the initial coarse emulsion in nanodroplets to yield nanospheres.

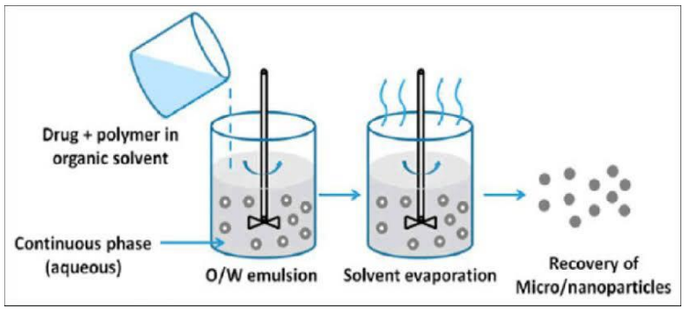


Figure:11- Solvent evaporation method

Solvent Diffusion Method

- Solvent diffusion method involves the dissolving of polymers or lipids and drugs in a volatile organic solvent by creating an emulsion O/W(oil in water) and diffuses the solvent into an aqueous phase, and causes the material to precipitate as nanoparticles.
- It prepares the nanoparticles by dissolving drug in a partially water-miscible solvent by emulsification it in aqueous phase.

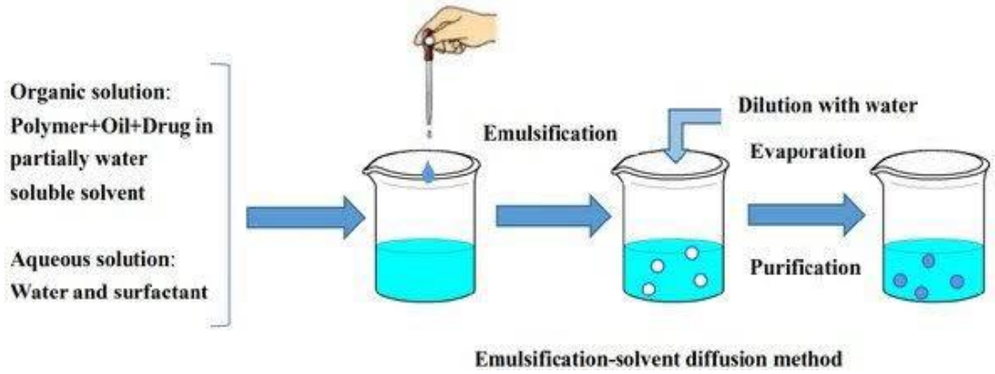


Figure:12- Solvent diffusion method

Supercritical Fluid Extraction Method

- Supercritical fluid extraction method is a technique which primarily using carbon dioxide, are efficient methods for producing standard-purity nanoparticles with controlled size and structure.
- It is an method used for the synthesis of metal and metal oxide nanoparticles.

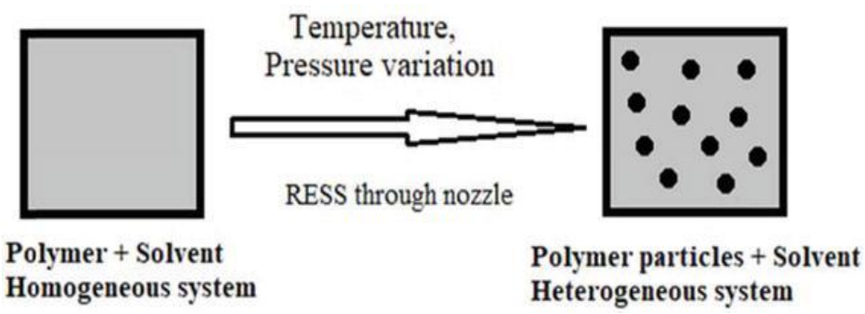


Figure:13- Supercritical Fluid Extraction Method

Melt Emulsification and Homogenization Method

- It is a method for creating nanostructured lipid carriers which are useful for low melting point components.
- This process involves combining an lipids at controlled temperature, repeatedly with high-speed homogenization.
- It is essential for producing solid-lipid nanoparticles and nanosuspensions.

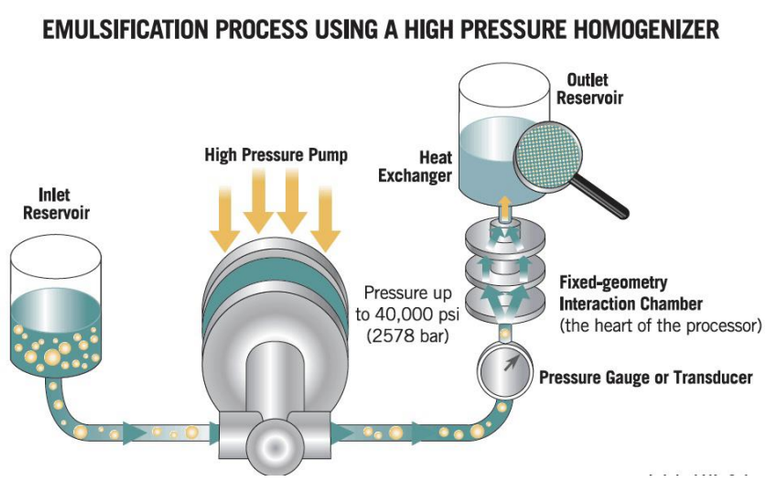


Figure:14- Melt emulsification and homogenization method

APPLICATION OF NANOPARTICLES [9,10]

- **Tumour targeting using nanoparticles drug delivery system**

It is a popular research in biomedical field which targeted ability of the inherent properties of nanoparticles based on the ligand receptors interaction have gained deeper understanding. Nanoparticles will reduces the drug exposure of the health tissues by limiting drug distribution to a specific targeted organs.

- **Gene delivery using nanoparticles drug delivery system**

The polynucleotide vaccines can works by the delivering genes encoding appropriate antigens to host cells where they can expressed, producing the antigenic proteins inside the surroundings of professional antigens presenting cells to initiate the immune responses.

- **Nanotechnology in anti-microbial**

It is the one of the earliest nanomedicine method use of nanocrystalline silver, which is an anti-microbial agents used for the treatment of wounds. Nanoparticles contains the nitric oxide gas, which are used to kill the bacteria.

- **Cell repair by using nanotechnology**

Nanorobots can be programmed to repair the specific diseased cells, the function is similar to the antibodies in our natural healing process.

CHALLENGES IN DEVELOPMENT OF NANOPARTICLES [11,12,13]

- **Scalability and Manufacturing**

The production of nanoparticles with the consistent quality standards remains a challenge . The transfer from lab-scale synthesis to large-scale synthesis manufacturing needs reproducibility, stability , and cost-effectiveness.

- **Safety and Regulatory approvals**

Regulatory authorities requires attentive safety assessments for nanoparticle based drug delivery systems. By understanding the potential toxicological effects, bio distribution and long-term safety profile of the nanoparticles is crucial.

- **Targeted delivery Specificity**

To achieve accurate and reliable targeting remains a challenge. The functionalized nanoparticles can increase targeting to specific cells or tissues, the variations in receptors expression can limit the efficacy of targeting strategies.

- **Biological barriers and Clearance**

Barriers such as, reticuloendothelial system and renal clearance can limit the circulation and accumulation of nanoparticles. Strategies to reduce these barriers and prolong nanoparticles circulation are required to optimize drug delivery efficacy.

- **Personalized medicine**

Customizing nanoparticles-based therapy to individual patients profile is emerging border. This requires the advancement in biomarker identification and diagnostic modeling.

CONCLUSION

Nanoparticle-based drug delivery system represents a promising boundary in the field of nanomedicine, offering unmatched opportunities to revolutionize drug delivery and improve therapeutic outcomes. The emergence of nanotechnology is likely to have a impact on drug delivery field, affecting about every route of administration from oral route to injectable. Advancement in nanoparticle design, synthesis have enabled precise control over drug release kinetics, biocompatibility and targeting specificity. The flexibility of nanoparticles allows for the encapsulation of wide range of a therapeutic agents, included small molecules, nucleic acids, proteins, and facilitating personalized medicine approaches and combinations treatments or therapies. Nanoparticle-based drug delivery systems offers several advantages over conventional drug delivery, including enhanced drug solubility, prolonged circulation and reduced systemic toxicity.

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