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A Review Article on Nano Drug Delivery System

J. Bharathi[1, 2], *Ekula Kalyani[2], Gedipalli Neelavathi[3], Poli. Kalyan[4]

[1*]Assistant Professor, Department of Pharmaceutics, Faculty of Pharmacy, Krishna Teja Pharmacy College, Tirupathi, Andra Pradesh-516101, India
[2]Bachelor of Pharmacy, Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupati Andhrapradesh-516101, India
Email: madhavisuresh470[at]gmail.com
[3]Bachelor of Pharmacy, Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupathi, Andhra Pradesh-516101, India
[4]Bachelor of Pharmacy, Krishna Teja Pharmacy College, Chadalawada Nagar, Tirupathi, Andhra Pradesh-516101, India

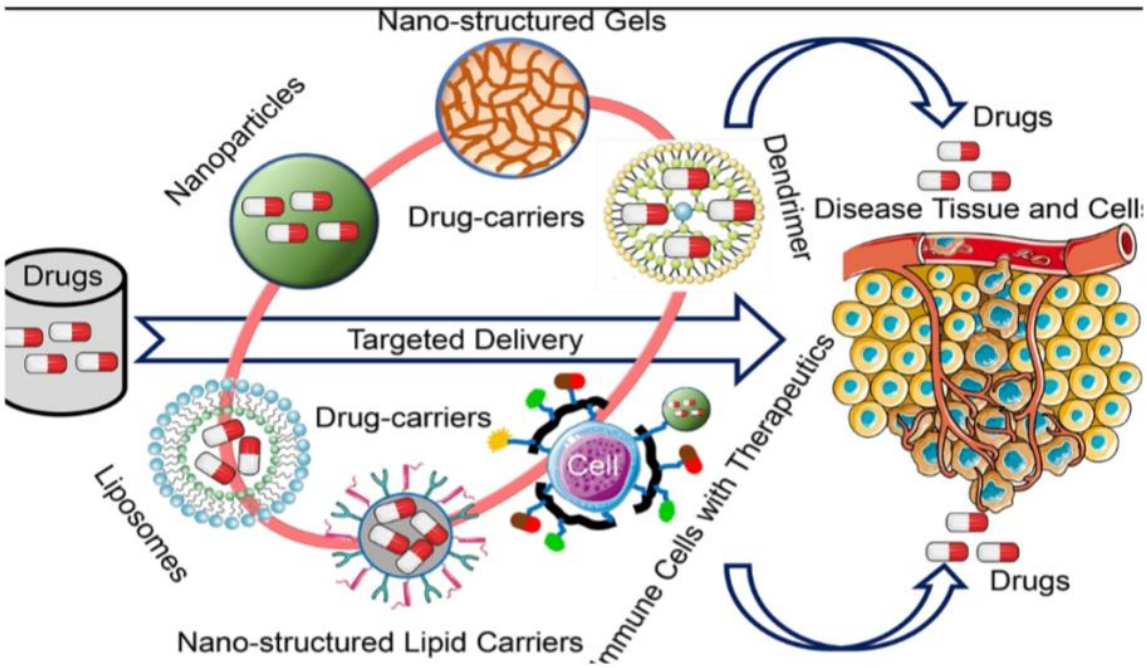
Abstract: ***Nanoscale carriers are used to effectively deliver therapeutic drugs at precisely targeted sites in a controlled manner, providing a number of benefits related to improved efficacy and minimizing adverse drug reactions. These nano-delivery systems overcome the issues with the conventional delivery method by providing precise, site-specific, target-oriented drug delivery with low toxicity, longer circulation time, high solubility, and long retention times in the biological system. Recently, structural characteristics, size manipulation, and selective diagnosis using disease imaging molecules have been thoroughly investigated in nanocarriers like dendrimers, liposomes, nanotubes, and nanoparticles. Materials in the nanoscale range are used as diagnostic instruments or to deliver therapeutic compounds to specific targeted regions in a controlled manner in nanomedicine and nano delivery systems. The use of nanomedicine in the treatment of various diseases has recently seen a number of notable applications. Due to a number of benefits, targeted medicine delivery has recently attracted increased interest. Among the numerous avenues investigated for precise medication delivery. Depending on the method of preparation, one can produce nanoparticles, nanospheres, or nanocapsules. Controlling particle size, surface characteristics, and the release of pharmacologically active substances are the main objectives when designing nanoparticles as a delivery system in order to achieve the drug's site-specific activity at the therapeutically ideal pace and dosing regimen. Present review reveals the Methods of preparation, characterization and application of several nanoparticulate drug delivery systems.***

Keywords: Nanoparticulate drug delivery system, Types of drug Targeting, Factors affecting on drug delivery, Types of Nanoparticles, Methods

1.Introduction

Systems for targeted administration and controlled release of medicinal drugs using nanoparticles are known as nanoparticle drug delivery systems. A modern drug delivery system should lower dosage and frequency while minimizing negative effects. Drug delivery systems at the nanoscale (NDDS) are quite unique. NDDS are unique because they frequently target particular cells in particular tissues or organs. They are unique in that the majority of them concentrate on chemotherapy for cancer. These NDDS have a size scale that varies from a few nanometers to several hundred nanometers. The number of NDDS with FDA approval has dramatically increased in recent years.

Graphical Abstract:



Cell-specific targeting can be accomplished by appending drugs to individually designed carriers. Late improvements in nanotechnology have demonstrated that nanoparticles [structures smaller than 100 nm in at least one dimension] have an incredible potential as drug carriers. [20-23] Because of their small sizes, the nanostructures show unique physicochemical and biological properties [e.g., an enhanced reactive area as well as an ability to cross cell and tissue barriers] that make them a favorable material for biomedical application.

2.Types of Targeting

2.1 Passive Targeting

Nanodrugs are able to accumulate in tumor tissues thanks to passive targeting, which takes advantage of the special pathophysiological features of tumor vasculature. Regularly, the pore count and extreme disarray of tumor arteries result in a defective lymphatic drainage system and widened crevice gap connections between endothelial cells. The "leaky" vascularization, which refers to the EPR impact, allows macromolecules to move up to 400 nm into the surrounding tumor zone. Additionally, the milieu around tumor tissue has a different EPR influence than healthy cells, a physiological characteristic that supports passive targeting. They need additional oxygen and nutrients due to the high metabolic rate of rapidly growing tumor cells. As a result, glycolysis is boosted to produce more energy, creating an acidic environment [56-60]. In light of this, pH-sensitive liposomes were modified to release therapeutic molecules at an acidic pH even though they were designed to be stable at a physiological pH.

2.2. Active Targeting

One way to get around the limitations of passive targeting is to attach affinity ligands-antibodies, peptides, aptamers, or tiny molecules that only bind to specific cell surface receptors-to the surface of nano carriers using a variety of conjugation chemistries. [81-86] The epitopes on the cell surface will let nano carriers recognize and bind to target cells through ligand-receptor interactions. [87-90] These receptors need to be highly expressed on tumor cells but not on normal cells in order to achieve high specificity.

3.Types of Nanoparticles

The classes of nanoparticles listed below are all very general and multi-functional; however, some of their basic Properties and current known uses in nanomedicine are described here;

1. Solid lipid Nanoparticles
2. Liposomes
3. Nanostructured lipid Carriers
4. Gold nanoparticles

3.1. Solid Lipid Nanoparticles:

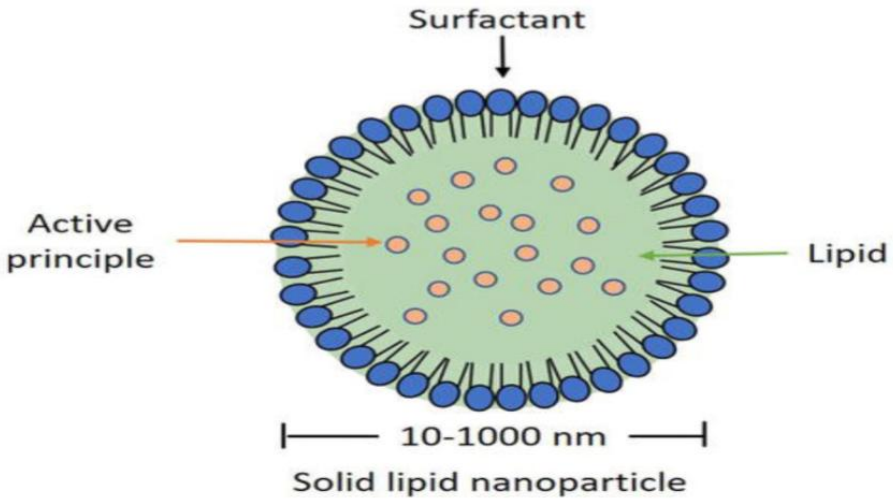


Figure 1: General Diagram of the solid lipid nanoparticles

For colloid drug delivery applications, SLNs primarily consist of lipids that are in the solid phase at room temperature and emulsifying surfactants, whose mean diameters range from 50 nm to 1000 nm. Small size, large surface area, high drug loading, phase interaction at interfaces, and other special features make SLNs stand out from other materials are appealing due to their improvement potential. Spray drying, high shear mixing, ultrasonication, and high pressure homogenization (HPH) are common techniques for creating SLNs. Fatty acids (such as palmitic, decanoic, and behenic acids), triglycerides (such as trilaurin, trimyristin, and tripalmitin), steroids (such as cholesterol), partial glycerides (such as glyceryl monostearate and glyceryl behenate), and waxes (such as cetyl palmitate) are solid lipids used in SLN formulations.

3.2. Preparation methods for solid lipid Nanoparticles:

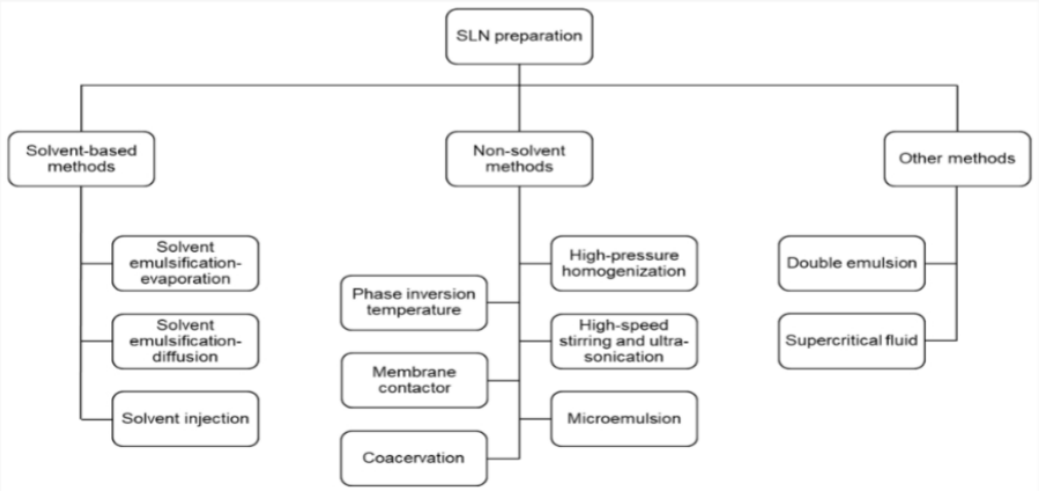


Figure 2: Classification of SLN preparation methods

A. Solvent based evaporation:

3.2.1. Solvent Emulsification-Evaporation Method: The solvent emulsification-evaporation method includes two steps: (i) preparation of Oil/water nanoemulsions and (ii) solvent evaporation. In this method, lipids and a drug are dissolved in a solvent or a solvent mixture to form the oil phase, which is, subsequently, Emulsified in an aqueous phase. The solvents are water-immiscible organic solvents, Such as dichloromethane, chloroform, cyclohexane, and toluene [88, 89]. After oil-in-water Nanoemulsions are formed, the organic solvent is evaporated. The solvent evaporation is, usually, carried out using a rotary evaporator or mechanical stirring. During solvent evaporation, the concentration of lipids in droplets increases gradually, resulting in lipid precipitation and the formation of SLNs.

3.2.2. Solvent emulsification diffusion: The solvent emulsification-diffusion method includes four steps: (i) Mutual saturation of water and an organic solvent with each other, (ii) Preparation of oil/water nanoemulsions, (iii) Dilution with water, and (iv) Solvent elimination. The first step produces Water-saturated solvent and solvent-saturated water, to obtain an initial thermodynamic Equilibrium of the water and organic phases. Therefore, in this method, organic solvents, Such as benzyl alcohol, butyl lactate, methyl acetate, ethyl acetate, and isopropyl acetate are used, due to their partial miscibility with water. In the second step, drugs and lipids are dissolved in the solvent, followed by the emulsification of both phases to form an oil/water Emulsion. In the third step, the emulsion is diluted with water by 5-10-fold. Upon dilution with water, the solvent diffuses into water, leading to the precipitation of lipids. As a result, SLNs are formed. The fourth step is to eliminate the solvent, usually by vacuum drying or Lyophilization.

3.2.3. Solvent injection: The solvent injection method was first used to prepare SLNs in 2003 [105]. It includes three steps: (i) preparation of the water phase and oil phase, (ii) solvent injection, and (iii) solvent removal. In this method, the oil phase is prepared by dissolving lipids and Drugs in a water-miscible solvent, such as ethanol, methanol, isopropanol, acetone, or a Water-miscible solvent mixture. The aqueous phase is a water solution of an emulsifier or an emulsifier mixture. In the second step, the organic phase is loaded into a syringe with a Needle and quickly injected into the aqueous phase, under continuous mechanical stirring.

Oil droplets are, immediately, formed at the injection site. Under solvent diffusion, lipid concentration within these droplets increases, leading to the formation of SLNs stabilized by the emulsifier. The third step is the removal of the solvent. Some modifications of the solvent injection method include a micro-channel with a cross-shaped junction [106] and a co-flowing micro-channel system. Some drugs have been loaded into SLNs using the solvent injection method, such as pueraria flavones ondansetron, Nalbuphine, and resveratrol.

B. Non solvent methods:

3.2.4: High pressure harmonization: The high-pressure homogenization (HPH) method is used to reduce the size of droplets and solid particles under extreme pressure conditions. The HPH method has the Advantages of organic solvent-free operation, short production time, and scale-up feasibility. This method can be classified into hot and cold homogenization. The hot HPH method includes three steps: (i) preparation of a coarse emulsion, (ii) homogenization under high pressure, and (iii) cooling. In the first step, drugs and lipids are melted at a Temperature typically 5-10 ◦C higher than the melting point of solid lipids. An aqueous Phase containing emulsifiers is preheated to the same temperature as the lipid melt. Two phases are mixed to produce a hot coarse emulsion. In the second step, the emulsion.

Is homogenized at the same temperature, using a homogenizer at 500-1500 bars for 3-5 cycles. Under high pressure, the liquid mixtures are pushed through a narrow gap (few Microns) of the homogenizer, at a high velocity (~1000 km/h), which results in high shear stresses and cavitational forces, to reduce the size of the droplets. The third step is toCool down the nanoemulsions to form SLNs. This method has been used to prepare SLNs loaded with

various drugs, such as celecoxib, atorvastatin, ketoconazole, Fluoxetine and ropinirole-dextran sulphate. The hot HPH method is unsuitable for preparing SLNs loaded with heat-sensitive or hydrophilic drugs.

The cold HPH includes two steps: (i) preparation of lipid microparticles and (ii) homogenization under high pressure. In the first step, drugs and lipids are mixed at a high temperature, to prepare a homogeneous dispersion of drugs in lipid matrices. The mixture is rapidly cooled down by dry ice or liquid nitrogen and, then, pulverized by a ball mill or a mortar to produce lipid microparticles (with size of ~50-100 µm). In the second step, the lipid microparticles are suspended in a cold aqueous solution containing Surfactants. This suspension is, then, homogenized at a cold condition (0-4 ◦C) over 5-10 cycles at 500 bars. This method is suitable for water-soluble drugs, to prevent drug loss during homogenization. Some methods have been used to minimize drug loss, such as adjustment of the pH of the aqueous phase, in the cases of drugs with pH-dependent Solubility or preparation of dug-lipid conjugates. The disadvantages of the Cold HPH method include large particles and laborious processes. This method has been used successfully to prepare SLNs loaded with toad venom extract, calf-thymusDNA and TRPsiRNA, and ondansetron.

3.2.5. High-Speed Stirring and Ultra-Sonication Methods: High-speed stirring (high-shear homogenization) is a straightforward and cost-effective. Method to prepare SLNs. This method includes three steps: (i) Preparation of water and lipid phases, (ii) Homogenization, and (iii) Cooling. In the first step, lipids and a drug are dispersed homogeneously at a high temperature (5-10 ◦C higher than the melting point of solid lipids), whereas an aqueous phase containing surfactants is prepared at the same Temperature. In the second step, the two phases are mixed and homogeneously dispersed by a high-shear mixer, to form a hot oil/water emulsion. The third step is to cool down this Emulsion to form SLNs. This method is, usually, combined with ultra-sonication. At the end of the second step, to reduce the size of the emulsion. The high-speed stirring and ultra-sonication methods have the advantages of organic, Solvent-free operation and ease of implementation. However, these methods are involved in high surfactant amounts, the exposal of drugs to high temperature, and the contamination of metals originating from sonicator probes. These methods have been successfully used to incorporate various drugs into SLNs, such as linagliptin, Quercetin and resveratrol, amphotericin B, buspirone, clozapine, Piribedil, primaquine, and astaxanthin.

3.2.6. Microemulsion Method: The microemulsion method includes two steps: (i) preparation of a Microemulsion and (ii) dilution. In the first step, drug and lipids are mixed at a temperature above the lipids' melting point. An aqueous phase containing surfactant is preheated to the same temperature and, then, added to the lipid phase under mild stirring, to form a Microemulsion. In the second step, the microemulsion is poured into a cold aqueous solution, under mechanical stirring. This process results in the formation of SLNs, Due to lipid precipitation.

3.2.7 Phase Inversion Temperature (PIT) Method: The PIT method is based on the use of non-ionic polyoxyethylated surfactants that have temperature-dependent properties. The ethoxy groups are highly hydrated at low temperatures, and, thus, the surfactants have a high hydrophilic-lipophilic-balance (HLB) Value. At high temperatures, the ethoxy groups are dehydrated, which decreases the HLB value of the surfactants and increases their lipophilicity. PIT is the temperature at which the surfactants have an equal affinity for aqueous and lipid phases. The PIT method includes three steps: (i) heating, (ii) cooling, and (iii) the precipitation of lipids. In the first step, drugs, lipids, water, and surfactant are heated to a temperature > PIT, to Form a water/oil emulsion. In the second step, the water/oil emulsion is rapidly cooled, to induce the formation of an oil/water nanoemulsion. The heating and cooling process can be carried out for several cycles (e. g., three cycles between 60 and 90 ◦C). The Third step is to cool the oil/water nanoemulsion, to precipitate lipids and form SLNs.

3.2.8. Membrane Contactor Method: The membrane contactor method requires the use of a specific membrane contactor. This method includes two steps: (i) preparation of a hot nanoemulsion by a membrane Contactor and (ii) cooling. In the first step, drugs and lipids are mixed at a temperature above the solid lipids' melting point. The lipid phase is, then, pressed through the pores of a membrane under the same temperature, to produce small lipid droplets. On the other side of the membrane, an aqueous phase containing surfactants flows tangentially to the Membrane surface and sweeps the lipid droplets away, to form a hot nanoemulsion. The second step is to cool down the nanoemulsion, to form SLNs.

3.2.9. Coacervation Method: The coacervation method includes three steps: (i) preparation of a micellar solution, (ii) addition of a coacervating solution, and (iii) cooling. This method uses alkaline salts of Fatty acids (e. g., sodium behenate and sodium stearate) as lipids. In the first step, lipids and drugs are dispersed in an aqueous solution of a polymeric stabilizer and heated, to Form a clear micellar solution of the lipid alkaline salts. In the second step, a Coacervating solution is added dropwise, to precipitate the lipids. The third step is to cool down the suspension, for complete lipid precipitation.

C. Other methods:

3.2.10. Double Emulsion Method: The double emulsion method can be carried out with or without organic solvents. This method includes three steps: (i) preparation of a water/oil emulsion, (ii) preparation of a water/oi/water double emulsion, and (iii) precipitation of lipids. In the first step, an aqueous solution containing drugs and stabilizers is emulsified in a water-immiscible Organic phase containing lipids or in solvent-free molten lipids, to Form a water/oil emulsion. In the second step, this emulsion is dispersed in an aqueous Phase, to form a water/oil/water double emulsion. In the third step, the double emulsions cooled down, to form SLNs. If an organic solvent is used, it is evaporated to Produce SLNs.

3.2.11. Supercritical-Fluid-Based Methods: Supercritical fluid (e. g., supercritical CO2) can be used to aid the preparation of SLNs. In the supercritical-assisted-injection method, supercritical CO2 is added in an organic phase, before solvent injection into an aqueous phase. Upon injection, lipids rapidly precipitate to form SLNs. Instead of solvent injection, the organic phase-supercriticalCO2 mixture can be expanded through a nozzle, to form SLNs. In the supercritical fluid extraction of emulsion method, an oil/water emulsion and supercritical CO2 are added to an extraction column, in a counter-current manner from the top and bottom, respectively. The supercritical CO2, quickly and entirely, extracts solvents in the oil phase of the emulsion, to for SLNs. These supercritical-fluid-based methods can provide uniform-particle-size distributions and high solvent-extraction efficiencies. However, these methods require organic solvents and expensive supercritical fluids. Some drugs have been loaded into SLNs by supercritical-fluid-based methods, such as campothecin and praziquante.

4.Liposomes

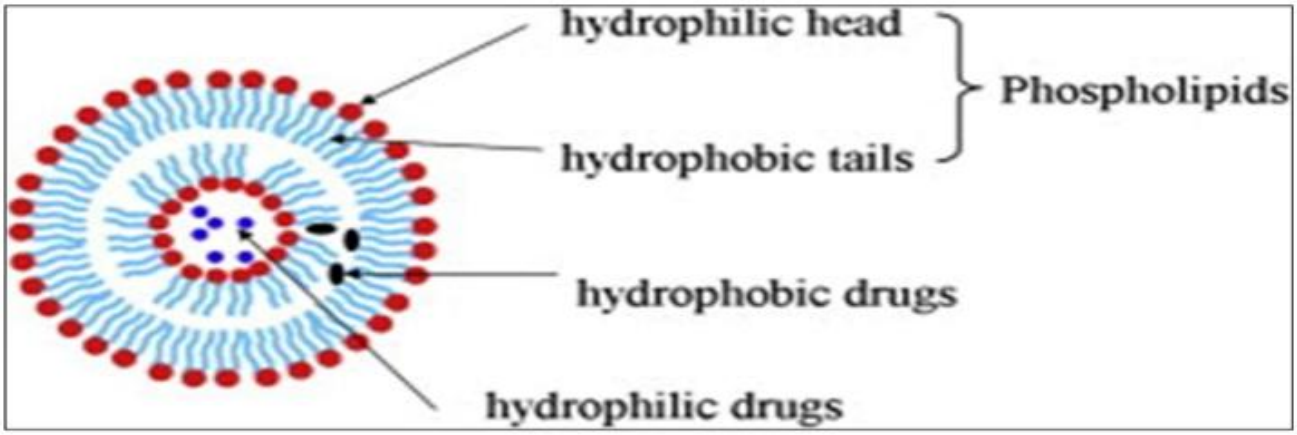


Figure 3: Structure of liposomes

The ejection of phospholipids results in the formation of liposomes, which are vesicular structures having an aqueous core encircled by a hydrophobic lipid bilayer. Because phospholipids are GRAS (generally acknowledged as safe) substances, the possibility of negative consequences is reduced. The hydrophobic bilayer prevents solutes, such as medicines, from passing through it; yet, hydrophobic molecules can be absorbed into the bilayer, allowing the liposome to transport both hydrophilic and hydrophobic molecule. Liposomes are valuable for medication delivery and cosmetic distribution applications because the lipid bilayer of these particles can fuse with other bilayers, such as the cell membrane, to facilitate the release of their contents. Nanoliposomes are another name for liposomes with vesicles that are in the nanometer range. From 15 nm to several lm in size, liposomes can have a single layer (unilamellar) or many phospholipid bilayer membranes (multilamellar) in their structure. Depending on their size range, unilamellar vesicles (ULVs) can be further divided into small unilamellar vesicles (SUVs) and large unilamellar vesicles (LUVs).

4.1 Preparation methods for liposomes:

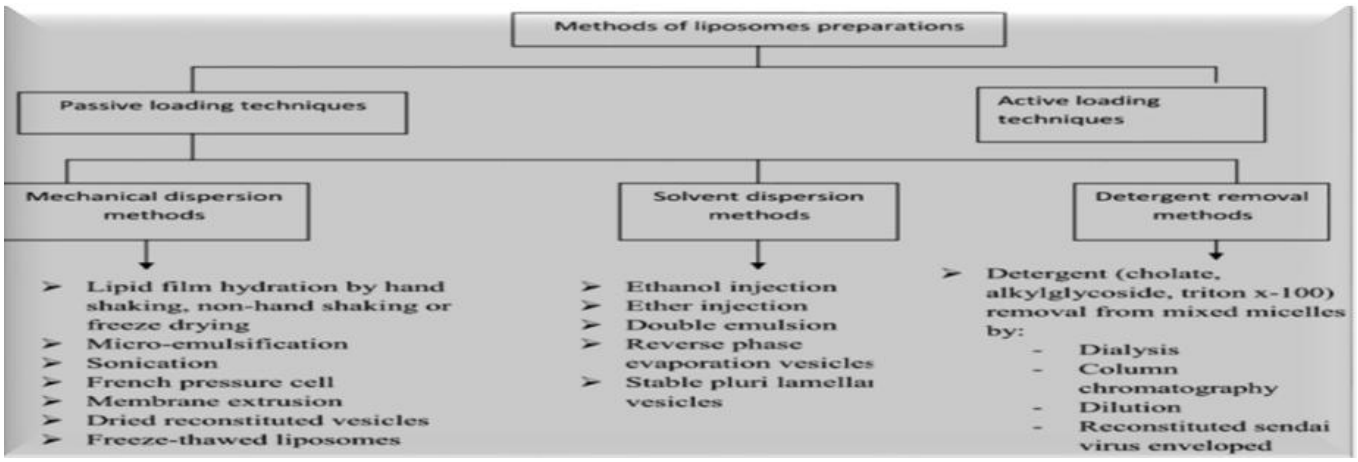


Figure 4: Classification methods for preparation of liposomes

A. Passive Loading Techniques

Mechanical dispersion methods:

4.1.1 Lipid hydration method: This is the most common Method of preparing MLV this method lipid solution was dried so that a thin film was formed at the bottom of RBF

and then film was hydrated by adding aqueous buffer and vortexing the Mixture. The hydration step is done at a temperature above the gel liquid crystalline transition temperature. The compounds to be encapsulated are added either to aqueous buffer or organic solvent depending upon their Solubility.

4.1.2 Micro emulsification: This method is used for preparing SLV. It can be achieved by microemulsifying lipid Compositions using high shearing stress generated from High pressure homogenizer.

4.1.3 Dried reconstituted vesicles: In this method liposomes are added to an aqueous solution containing drug or mixed with lyophilized protein, followed by dehydration of Mixture.

4.1.4. Freeze thaw method: IN this method SUVs were frozen rapidly by slow thawing technique. The formation of Unilamellar occurs due to this reason.

B. Solvent Dispersion: A lipid solution of ethanol was added to A

4.1.5. Ethanol injection: an aqueous buffer which immediately forms MLV.

4.1.6 Ether infusion: A solution of lipids dissolved in Diethylether and is slowly injected to a solution of the Material to be encapsulated at temperature 55-60◦ C29.

4.1.7 Detergent: Lipids were solubilized by detergents at their critical miscelles concentration. As detergent is removed, miscelles become richer in phospholipids and finally combine to form LUVs.

C. Active Loading Techniques

4.1.8 Proliposomes: In this method lipid and drug were coated onto a soluble carrier to form free flowing granular Material in pro-liposome which forms an isotonic Liposomal suspension on hydration30.

4.1.9 Lyophillization: The removal of the products that are Thermolaible.

5.Nanostructured lipid carrier's

Nanostructured Lipid Carriers are made from a mixture of solid and liquid lipids, however at body temperature, the particles are solid. Lipids are adaptable molecules that can build variously structured solid matrices, such as the lipid drug conjugate nanoparticles (LDC) and nanostructured lipid carriers (NLC), which have been developed to increase drug loading capacity. The solidified emulsion (dispersed phase) technologies are the foundation of NLC production. Due to drug ejection upon polymorphic change during storage, NLC may have an inadequate loading capacity, especially if the lipid matrix contains identical molecules.

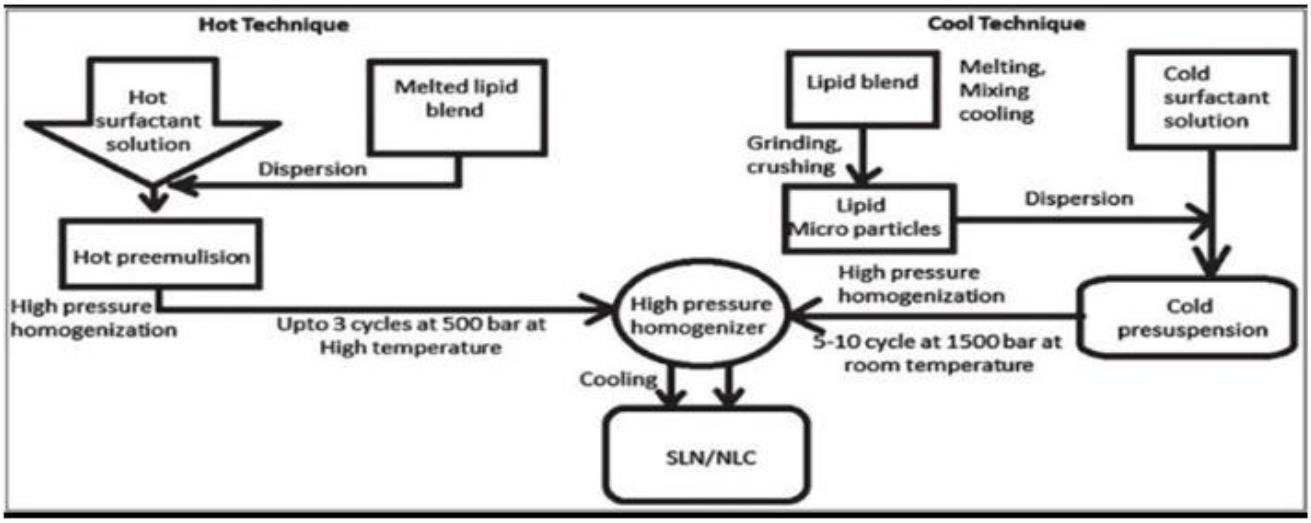


Figure 5: Nanostructured lipid Carrier

5.1 Preparation Methods for Nanostructured lipid Carriers

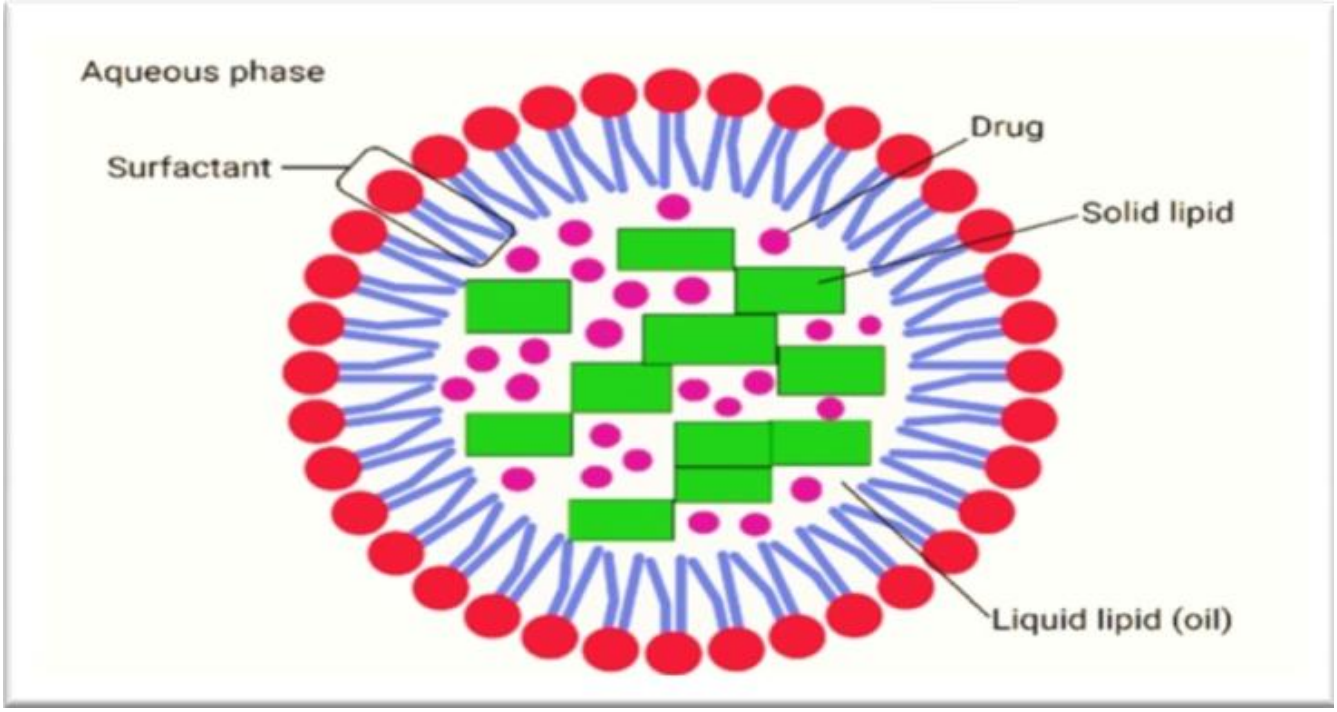


Figure 6: Schematic overview of the hot and cold homogenization techniques for NLC

5.1.1. High-pressure homogenization technique: High-pressure homogenization technique is one of the most reliable and powerful techniques for the large-scale production of Nano lipid carriers, lipid-drug conjugate, SLNs, and parenteral emulsions. In high-pressure homogenization technique, high pressure is introduced to push the lipid (100-200 bars) through a narrow gap of few micron ranges. So, shear stress and cavitation are the forces that cause the disruption of particle to submicron range. Normally, the lipid contents are in the range of 5%-10%. Basically, there are two approaches for production by high-pressure homogenization, hot and cold homogenization techniques. [31] For both the techniques, the drug is dissolved in the lipid that is being melted at approximately 5°C-10°C above the melting point.

5.1.2. Hot homogenization technique: In this technique, the drug along with melted lipid is dispersed under constant stirring by a high shear device in the aqueous surfactant solution of same temperature. The pre-emulsion obtained is homogenized by using a piston gap homogenizerand the obtained nanoemulsion is cooled down to room Temperature where the lipid recrystallizes and leads to Formation of nanoparticles [figure 6]

5.1.3. Cold homogenization technique: Cold homogenization technique is carried out with the Solid lipid that contains drug. Cold homogenization has been developed just to minimize the problems of the hot Homogenization technique, such as temperature-mediated Accelerated degradation of the drug payload, partitioning, and hence loss of drug into the aqueous phase during Homogenization. In the proceeding step the drug is cooled rapidly using liquid nitrogen or dry ice for drug distribution in lipid matrix as shown in Figure 7. Cold homogenization minimizes the thermal exposure of the sample.

5.1.4. Microemulsion technique: The lipids (fatty acids or glycosides, e.g., stearic acid) are melted, and the drug is incorporated in the molten lipid. A mixture of water, cosurfactant (s), and the surfactant is heated to the same temperature as the lipids and added under Mild stirring to the molten lipid. This microemulsion is then Dispersed in a cold aqueous medium under mild mechanical Mixing of hot microemulsion with water in a ratio in the range 1: 25-1: 50. This dispersion in cold aqueous medium leads to Rapid recrystallization of the oil droplets.

5.1.5. Double-emulsion technique: In double-emulsion technique, the drug (mainly hydrophilic Drugs) is dissolved in aqueous solution, and further emulsified in melted lipid. The primary emulsion is stabilized by adding Stabilizer that is dispersed in aqueous phase containing Hydrophilic emulsifier, which is followed by stirring and Filtration. Double-emulsion technique avoids the necessity to melt the lipid for the preparation of peptide-loaded lipid Nanoparticles, and the surface of the nanoparticles.

6.Gold Nanoparticle's

Goldparticles of a greater size are a yellow inert solid, whereas gold nanoparticles (GNPs) are a wine-red complex having antioxidant capabilities. GNPs come in a variety of shapes, including suboctahedral, spherical, octahedral, icosahedral multiple twined, decahedral, multiple twined, tetrahedral, irregular shape, nanotriangles, hexagonal platelets, nanorods, and nanoprisms. Their sizes rangefrom 1 nm to 8 m. High-molecular-weight active drugs can be delivered more effectively and have better skin permeability thanks to GNPs' capacity to interact with the skin barrier. GNPs are thought to be potential options for transdermal delivery system optimization and skin immunization. Further study is needed to determine the safety of GNPs for

transdermal delivery methods. Delivery and programmed release of therapeutic materials to Specific physiological targets is a key challenge for molecular and macromolecular therapeutic.

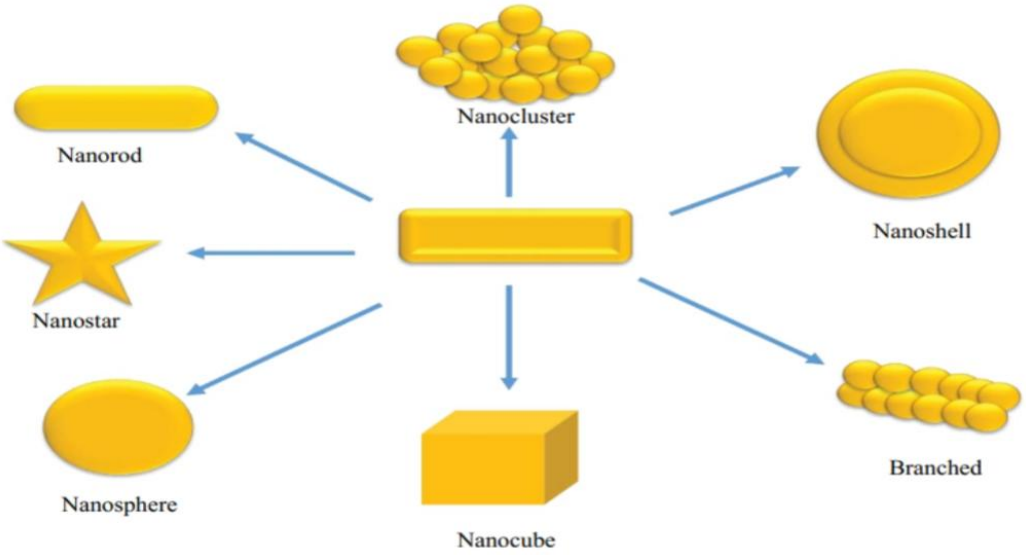


Figure 8: Gold Nanoparticles

6.1 Preparation methods for gold nanoparticles:

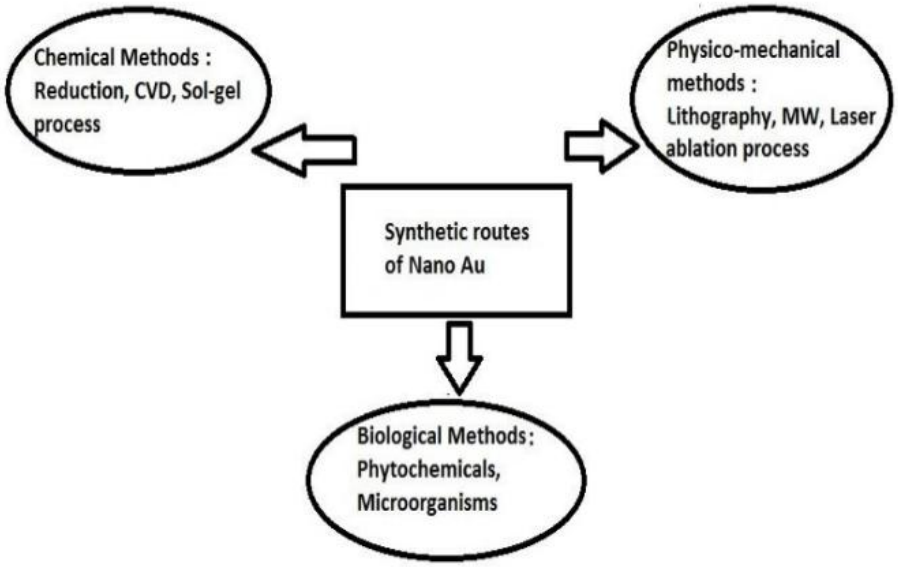


Figure 9: Different methods for synthesis of Gold Nanoparticles

6.1. Chemical method: Chemical technique was suggested by Gimenez et al. to prepare Au/NPs by the reduction process of the HAuCl4 Through a solution of thiolated chitosan. The method Of thermal citrate reduction used in the preparation of Au/NPs via Raman spectroscopy (SERS) by using inositol hexakisphosphate (IP6) To reduce HAuCl4 [53]. In addition, the preparation of Au/NPs is by the trisodium citrate and hydrogen tetrachlorocuprate (III) tetrahydrate (chloroauric acid). Au/NPs can be grown in encapsulated immersed in polyethylene Glycol dendrimers and reduced by formaldehyde under near infra-red. Gold nanoparticles are prepared by utilizing peptide-biphenyl Hybrids (PBHs) as a stabilizer for gold and in this method the size range 1.8 to 3.7 nm was reported. The dendrimers/Au nanoparticles can 1.8 be prepared by the reduction of a solution of HAuCl4 and sodium borohydride. The synthesis Au/NPs with size less than 10 nm can be by two various thiols involved ethylene glycol and dodecanethiol.

6.2. Biological method: In addition, a new method in green chemistry For the synthesis of Au/NPs has been recorded, in which Au/NPs were Dissolved in NaCl solution from the bulk gold substrate by using natural Chitosan without any stabilizer and reductant. Another green Synthesis method of Au/NPs with size from 15-80 nm was reported. In This approach, HAuCl4 Was used as a precursor and reduced by utilizing Citrus fruit juice extracts (Citrus limon, Citrus reticulate and Citrus Sinensis). The edible mushroom was also used for the preparation Of Au/NPs by light power.

6.3. Physical methods: The γ-irradiation technique is one approach for the synthesis of Au/NPs with uniform size from the range 5-40 nm and high purity, using polysaccharide alginate as stabilizer. The technique of microwave irradiation was used to prepare Au/NPs by reducing agents such as citric acid and a binding agent such as cetyltrimethyl ammonium bromide (CTAB). Furthermore, Au/NPs are prepared by using heat or photochemical reduction, and reduction of HAuCl4 by citrate, tartrate, and malate. A common method of photochemical reduction has been recorded for the synthesis of gold-polyethylene glycol nanoparticles by polymerization reactions with size 10-50 nm. Furthermore, in this approach, gold salt is reduced by radical formation coated with polyethylene glycol diacrylate by UV-reaction. One of another method, synthesis porous Au/NPs from alloys of gold is by using HAuCl4 and AgNO3 as precursors, then reduction by NaBH4 as a reducing agent. After that, de-alloying can be achieved by nitric acid.

7.Conclusion

Nanoparticles represent a promising drug delivery system controlled and targeted release. The emergence of Nanotechnology is likely to have a significant impact on drug delivery sector, affecting just about every route of Administration from oral to injectable. In addition, the payoff for doctors and patients should be lower drug toxicity, reduced cost of treatments, improved bioavailability, and an extension of the economic life of proprietary drugs. The Foregoing show that nano particulate systems have great potentials, being able to convert poorly soluble, poorly Absorbed and labile biologically active substance into promising deliverable drugs. Further advances are needed in order to turn the concept of nanoparticles technology into a realistic practical application as the next Generation of drug delivery system. This would allow earlier and more personalized diagnosis and therapy, improving the effectiveness of drug treatments and reducing side effects.

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