A Review On Pharmacological Action, Techniques And Stability Study Of Solid Lipid Nanoparticles

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Abstract
The range of drug delivery technology is broad, and it is being developed at an incredible rate. The two main substances widely supplied to target areas are variously manufactured nanoparticles and medications with poor pharmacokinetic and solubility profiles. Nano lipid dispersions are the best delivery mechanisms among colloidal carriers since they are harmless and biodegradable. Due to their biodegradability, nanostructured lipid carriers and SLNs are non-bio toxic. Additionally, they are very stable. Their morphology, structural properties, preparation ingredients, production processes, and characterization using various techniques.

Keywords: investigation of stability, pharmacological effect, and solid lipid nanoparticles

1. INTRODUCTION

Solid lipid nanoparticles (SLNs) are introduced as an effective technique of carrier for rectifying water-soluble and dynamic medications. Colloidal particles of a size between 10 and 1000 nm are known as nanoparticles. They are created from artificial natural polymers with a focus on reducing lethality and enhancing drug delivery.[1,2] They have developed as a versatile replacement for liposomes as a means of drug administration. They are best suited to maximize sedate delivery and decrease lethality and are created from synthetic or special polymers.[3] They could potentially enhance pharmaceutical execution, which makes them attractive.[4] Solid biodegradable lipids serve as the matrix of solid lipid nanoparticles (SLN), which are aqueous colloidal dispersions.[5,6] For a number of delivery routes, SLN formulations have been developed and extensively characterized in-vitro and in vivo.[7]

Solid lipid nanoparticles are one of the few different potential colloidal transporter systems as an alternative to polymers, in contrast to the oil-in-water emulsion utilized for parenteral feeding. The liquid lipid in the emulsion has been replaced by a solid lipid nanoparticle.[8,9]

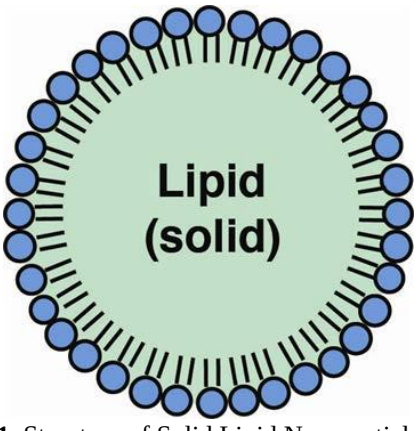

Figure 1. Structure of Solid Lipid Nanoparticle (SLN).

1.1. Advantages of SLN

- Small estimate and generally contract measure dissemination that provides opportunities for SLNs to deliver medication on-site
- Relevant traditional emulsion-making methods
- It is possible to stop-dry powdered detailing.
- It is possible to provide dynamic medication gradually over a long period of time.
- outstanding biocompatibility
- increase in pharmacological stability

- Excellent reproducibility using as the readiness process a clever high-weight homogenization technique.
- elevated and high drug content.
- Avoiding natural solvents is a priority.
- Large-scale generation and cleanup that is feasible.[10,11,12]

1.2. Disadvantages of SLN

- limit of poor sedate stacking.
- drug ejection following a polymeric shift while there is capacity.
- erratic gelation propensity.
- due to distributional effects throughout the production process, hydrophilic medicines have a low capacity to stack.[13,14]

1.3 DIFFERENT TYPES OF NANOPARTICLES

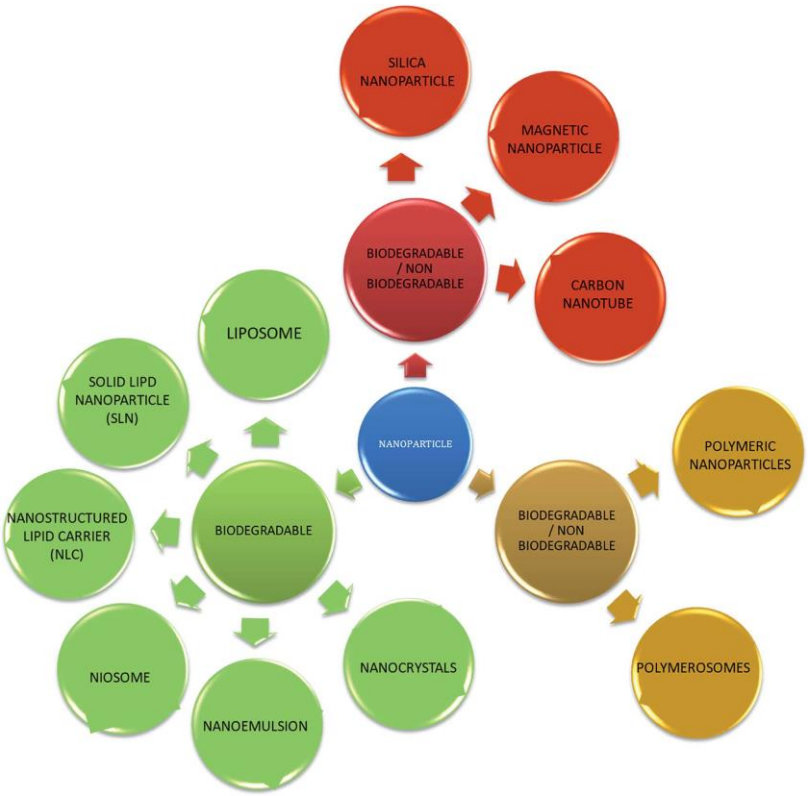

Figure 2. Types of nanoparticles

1.4 NANOPARTICLE CLASSIFICATION

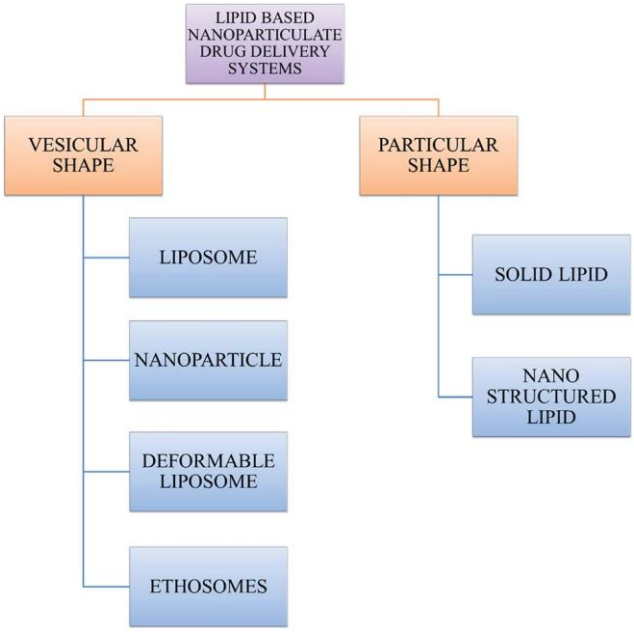

Figure 3. SLN classification

1.5 SLNs FORMULATION TECHNIQUES

1. High pressure homogenization techniques

For the production of parenteral emulsions, a high-pressure homogenizer is used. This technology is well established and very well accepted for the large-scale productions of nanoparticles. Lipid nanoparticles have been prepared by high pressure homogenization techniques. Two type of homogenization is used cold and hot for the preparation of nanoparticles. The lipid is been melted in both the process and the active compound is been dissolved and dispersed in high pressure homogenization. Through a narrow gap high pressure of liquid is been pushed (100-2000 bar). The forming particles may be disrupting by high shear stress and cavitation forces which may down the submicron range. This technique is used for the production of lipid nanoparticles. This technique is also used for the manufacture of parenteral lipid emulsion for long period. Other available technique may produce the problems. In curtained conditions, the high energy may affect the temperature and pressure of the system.[15,16]

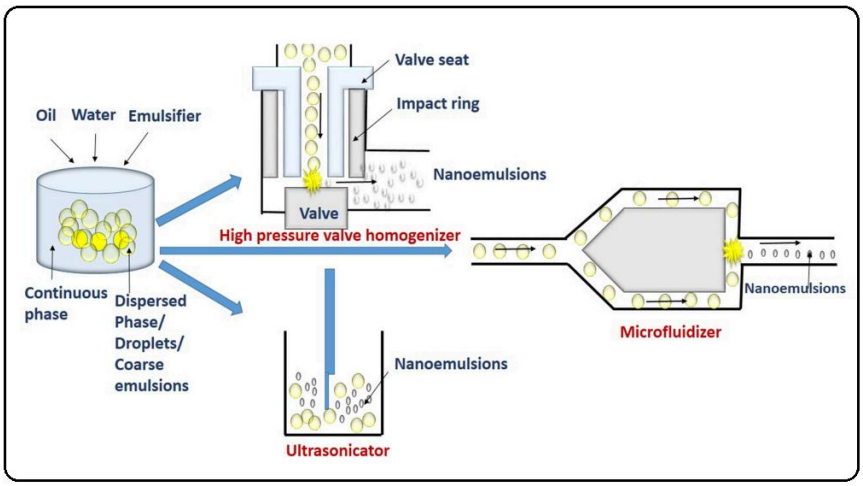

Figure 4. High pressure homogenizer

2. Hot high pressure homogenization technique

For the preparation of hot homogenizer, the loaded drug of pre-emulsion of lipid melts and a solution of emulsifier with high-shear was mixed by the help of a device. High melting point lipid is been used for pre-emulsion. after that cooling down the temperature of lipid may produce lipid nanoparticle. Hot aqueous surfactant is been used for the dispersion of melted lipid along with the drug at high-speed stirring. Then this pre-emulsion is been passed through high-speed homogenization to form the nano emulsion. This technique is most frequently applied for the formation of nano-particles. The lipophilic matrix and the drugs which are insoluble may entrapped. The high temperature is been short on the exposure time in hot high-pressure homogenizer and used for the compounds which are temperature sensitive. This process is not used for hydrophilic drugs. The lipid phase drugs may show the low encapsulated in melted lipid phase. [17,18]

3. Cold high pressure homogenization technique

The solid lipid drug has contained microparticles and then it may disperse into the emulsifier in hot homogenization. In this technique, the subject is been homogenized by low and may below the temperature. In cold homogenization, the melting point is been higher and the drug is been dissolved into it. For cool down this system liquid nitrogen and dry ice is been used. Ball and mortar milling is used for the lipid mass grounded for the formation of lipid microparticles (50 to 100 µm). These microparticles are used for the formation of microemulsion by using cold surfactant and continues stirring. A high-pressure homogenizer is been used for the passing of this substances below the room temperature. By this the microparticles may broke the nanoparticles. The initial step for the melting of lipid may be minimizing the thermal exposure. These were applied for the temperature sensitive compound. The incorporation of hydrophilic compounds. It may partition the liquid-liquid phase. In low solubility of the drug water can be replaced by liquids. Oil and PEG with low molecule weight has minimize the hydrophilic compound loss in aqueous dispersions. Cold high pressure homogenization technique is used for the preparation of lipid particles with higher PI and hot high pressure homogenization technique is used of the particle size. These cycles may be reducing the particle size and polydispersity minimize.[19,20]

4. Melt emulsification ultrasound homogenization technique

For the preparation of lipid carrier's hot homogenization technique is used. For this appropriate device is been used. Ultrasonication is been used instead of high-pressure homogenization for the production of lipid nanoparticles. For size reduction, this technique is used. In which the cavitation bubbles will be generated in extreme conditions. Ultrasonication is been used in place of homogenizer. For the operating parameter standardizing by the use of ultrasonic process. It is fast and highly reproducible. The parameter must be optimized such as temperature, ultrasonication time and power. These may be used for the large-scale production and self-cleaning. The in homogenizers are applied for power distribution as compared with high pressure homogenizers. It has small size of homogenizing gap.[21,22]

5. Microemulsion technique

This technique is been used in modern day time for the formulation of lipid nanoparticles. The preparation of nano emulsion is done by adding the excess amount of cooling condition in hot microemulsion this may broke the system and

it may convert into nano-emulsion. it may recrystallize the oil and form lipid particles. These may contain the drug mixer by the surfactant and cosurfactant in aqueous phase in the same temperature and form microemulsion. Excess of cold water is been used for the dilution of microemulsion. It is been convert into nano-emulsion by using recrystallization of lipid phase particles. Reduction in temperature and dilution with water may break the microemulsion region. Microemulsion composition, temperature, dispersing device, low temperature water and lyophilization are the parameter used for the formation of nano-particle. Advantages of these are the production of energy, scale-up the production of lipid nanoparticle. This technology has some disadvantages such as particle dilution suspension by water, excess water removal. Due to high concentration of surfactant and co-surfactant the regulatory concern may increase. dialysis, ultrafiltration or ultracentrifugation is used for the removal of surfactants.[23,24]

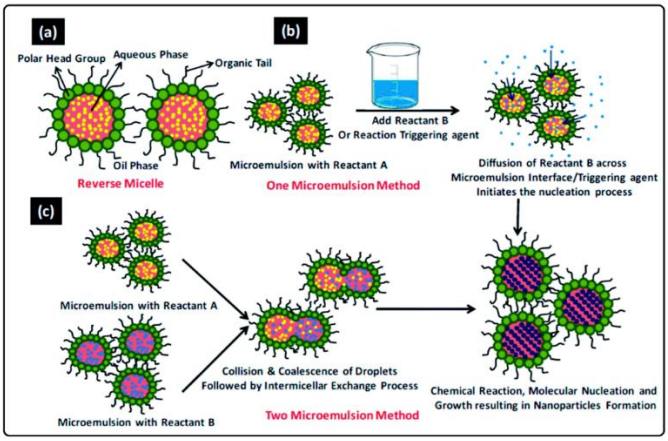

Figure 5. Microemulsion technique

6. Emulsification-solvent evaporation technique

Solvent evaporation technique is used in the o/w emulsions for the production of polymeric nanoparticles and microparticles. In this technique the lipid is been dissolved into the organic solvent. Under reduced pressure these emulsifiers may evaporated from aqueous phase. These particles may get evaporated from the and the lipid gets precipitated these may form nanoparticles. Organic solvent is used for the dissolved of lipid and the drug is been dissolved into the solution. By using mechanical stirring, this emulsifier is been dissolved into o/w emulsion. evaporation is been used for the removal of this substances. The particle aggregation is been used for the solvent evaporation. Heat is been avoidance during formulation is the one of the advantages. Some problem is been originated by solvent residues. Lyophilizer, ultra-filtration and evaporation is used for the solubility of lipid. 100nm is the particle size of a nanometric. [25,26]

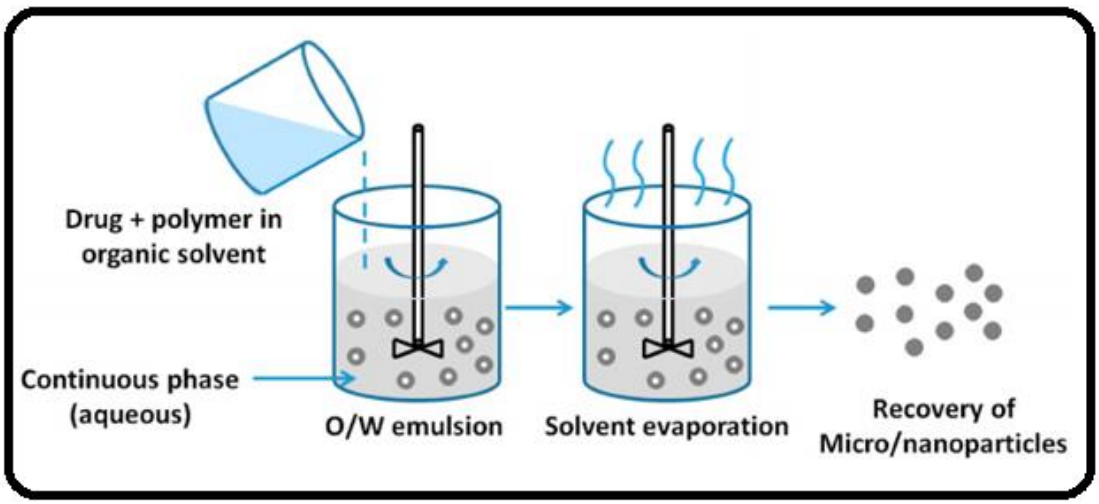

Figure 6. Emulsification-solvent evaporation technique

7. Solvent displacement or injection technique

For the preparation of liposomes and polymeric nanoparticles solvent displacement technique is been used. In modern day time, this technique is used for the preparation of lipid nanoparticles. This may be depending on precipitation of lipid in solution. The solvent is mixed into the aqueous phase by the addition or not addition of surfactant. In this process organic phase o/w emulsion is been mixed with aqueous phase by magnetic stirrer. The active component may be dissolved into this phase and the solvent which are not miscible with solvent. Surfactant is been added into aqueous phase. Solvent is removed from lipid nanoparticle by distillation process. The size of the particle must be depending on injected amount, concentration of lipid, emulsifier concentration. Some advantages are organic solvent acceptable, did not need high

pressure homogenizer, handling is easy, production process is fast. Some disadvantages are organic solvent which are used as an excipient use in formulation.[27,28]

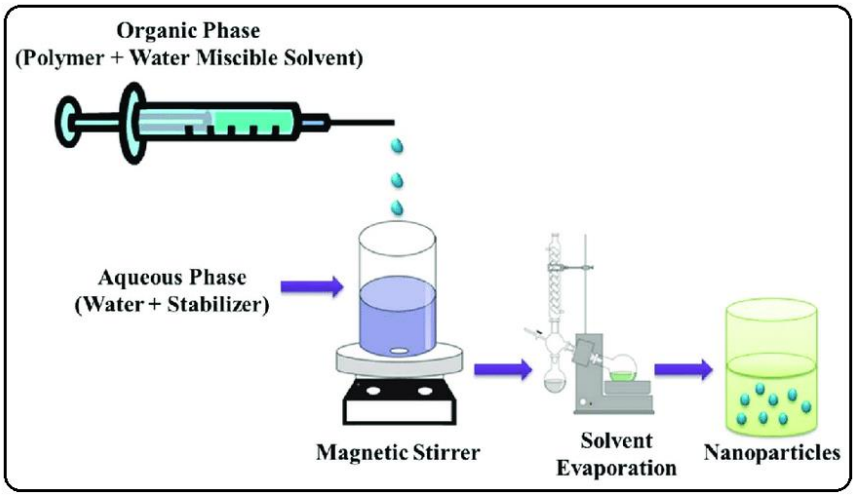

Figure 7. Solvent displacement or injection technique

8. Emulsification-solvent diffusion technique

For the production of polymeric nanoparticle from synthetic polymers through precipitation is done by emulsification-solvent diffusion technique. It is also used for the preparation of SLN and NLC. Solvents which are water miscible are used in this process. Saturation with water is ensure both the thermodynamic equilibrium. Then after lipid is been added into this water and it is been emulsified in aqueous surfactant solution. In continuous phase, due to the addition of excess water the organic solvent of emulsion droplets may form lipid nanoparticles. The equilibrium thermodynamic of two liquid is partially soluble in o/w emulsion. saturated solvent is been used for the dissolution of lipid. For the formation of o/w emulsion this emulsifier is been emulsified in aqueous solution which may contained the surfactant by mechanical stirring. When the solvent is been diffused an external phase is formed and the lipid is been started precipitating. Ultra-filtration and distillation were eliminated by solvents. After the removal of organic solvent, a lipid nanoparticle is formed. Around 100nm of particles is been achieved by this technique.[29,30,31]

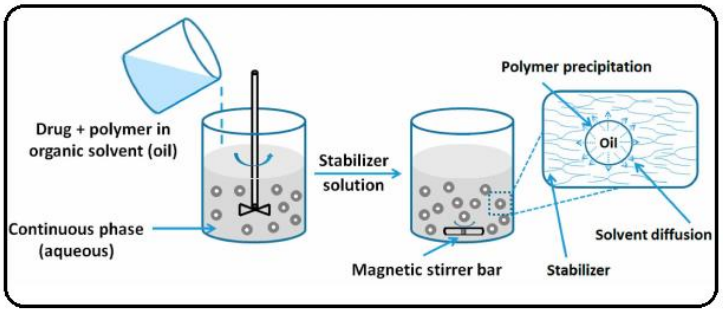

Figure 8. Emulsification-solvent diffusion technique

9. Phase inversion technique

This modern technique is been used for the preparation of lipid nanoparticles. These may be prepared by two techniques:1. Use of magnetic stirring for the addition of formulation components and heating cooling cycle. 2. These may be diluted in low temperature.

All the components like lipid surfactant and water must be well stirred at magnetic stirring. There are three cycles of heating and cooling is done. It should be raised from room temperature to 85^0C and then again back to 60^0C these may be done at the rate of 4^0C/min. by this process inversion of emulsion is done. Cold water is been diluted due to the introduction of irreversible shock these systems may be break down and the cold water is been induced for the dilution and maintained of elevated temperature. These dilutions of fast cooling process may form lipid particles which are nano metre range for the aggregation of particles a slow magnetic stirring is applied. These techniques are useful to the thermolabile drugs. The degradation of thermal is not occurred if the heating periods are very short. In this technique, the organic solvents are not used. There are some variations in formulation content proportion which may influences the size parameter.[32,33]

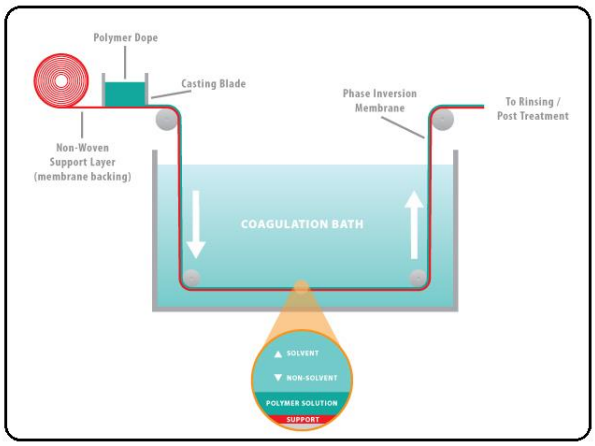

Figure 9. Phase inversion technique

10. Film ultrasonication dispersion technique

Sonication and high-speed stirring are been used for the preparation of lipid nanoparticles. For the formation of lipid phase an evaporation of solvent as well as ultrasonic dispersion is also done in the presence of aqueous surfactant solution in elevated temperature. After that the cooling is done for the formation of nanoparticles. Some advantages of these technique are their preparations are easily available in every lab. Disadvantages are border particle size distributers are in the micrometre range physical stability, particle growth is occurs by the use of ultrasonication a chances of metal contamination is occurs.[34,35]

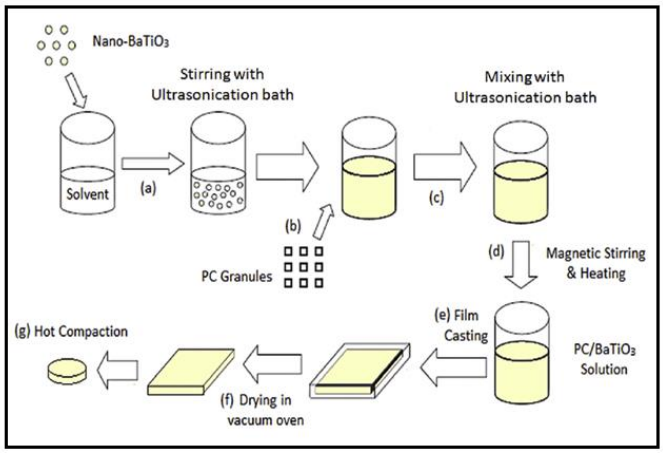

Figure 10. Film ultrasonication dispersion technique

10. Multiple emulsion technique

These are the modern technique. In which the emulsification-evaporation method is been modified. w/o/w double emulsion is used. For the preparation of hydrophilic drug encapsulation of SLN, the use of emulsification due to solvent evaporation. In w/o/w double emulsion, stabilizers are also used for the prevention of external water by solvent evaporation. These technique molecules like peptides and proteins.[36,37,38]

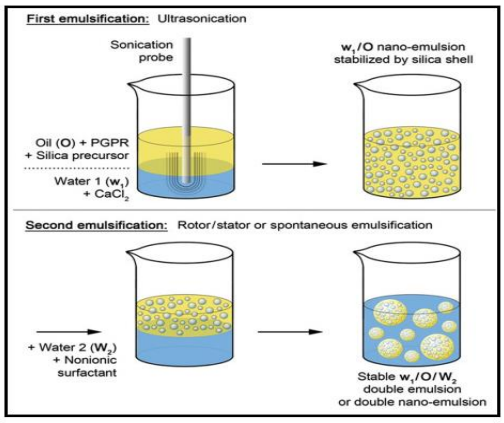

Figure 11. Multiple emulsion technique

11. Membrane contactor technique

The lipid is been passing through the pores of the membranes due to the high pressure which is higher than melting temperature of lipid. The minute droplets are been formed by the lipid phase is pressed through the membrane pores. The droplet is been formed at the outlets due to the aqueous phase inside the membrane module sweeps. SLN is been formed when these are cool at room temperature. The size and lipid flux is been affected at SLN due to aqueous and lipid phase temperature, circulating aqueous phase speed, pressure of lipid phase and membrane pore size. These are some advantages of these are simple procedure, the size of SLN is been appropriate at the parameter process and ability of scale up.[39,40]

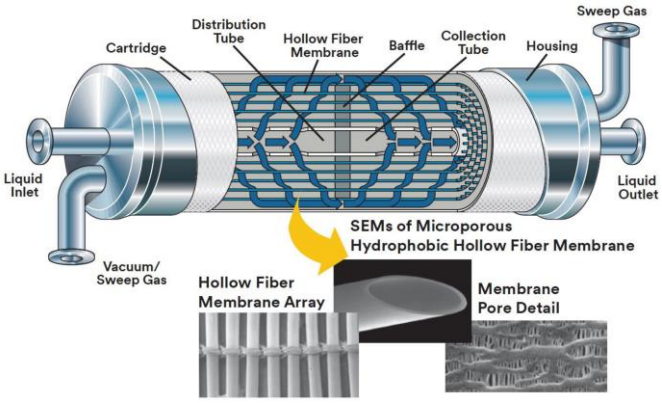

Figure 12. Membrane contactor technique

12. Supercritical PGSS technique

In modern day time these techniques are used for the production and preparation of SLN which contains supercritical carbon dioxide. These techniques are one step method which may encapsulating the drug into the organic free lipid particles. Carbon-dioxide is used for this technique. In this procedure the supercritical carbon dioxide ($ScCo_2$) is been dissolved into a bulk of lipid drugs, through a micron cone shaped nozzle may be used for the subsequent quick expansion of pressure release. It may cause meet atomization. The complete gas evaporation and SLN precipitation. Some advantages are one step process, there are no need for organic solvents. It may do at low temperature conditions. It has some disadvantages like nozzle is been blocked frequently in hydrophilic drugs. This machinery is very costly.[41,42]

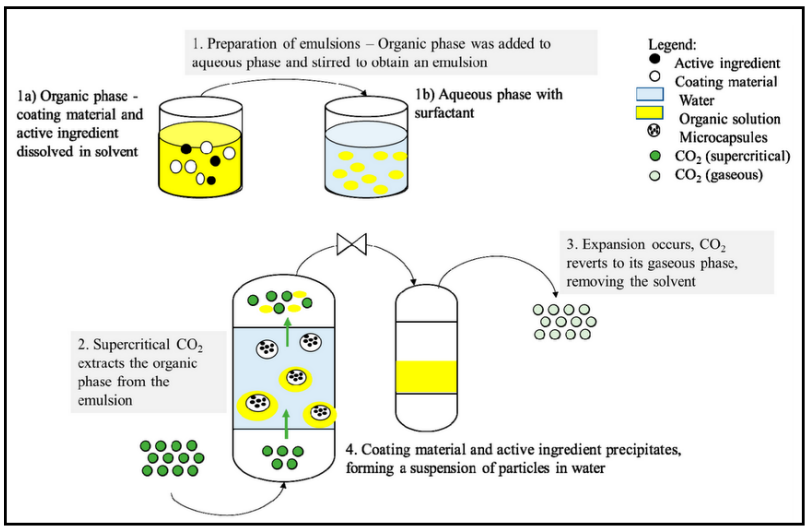

Figure 13. Supercritical PGSS technique

1.6 PHARMACOLOGICAL ACTIVITY OF SLNs

In recent era, nanotechnology paly a most important role. These may be used in drug delivery system. These are most innovative and crucial in pharmaceutical research. SLNs is used as a carrier for drug delivery system for a specific site. These may increase the interest and improved the pharmacokinetic as compared to traditional drug delivery system. SLNs are used in topical administration, intravenous administration, protein peptide delivery, Targeted dug delivery and ocular drug delivery. The most challenging part of NDDS are the targeting the brain for the delivery of medicaments. 98 to 99% of drug are not cross the blood brain barriers. SLNs have the lipid behaviour and has a effective nanometre size range to the targeted drug delivery system.[43,44]

1.7 STABILITY AND STORAGE OF SLNs

SLNs are more stable. It should be last up to three years. This is because of the presence of lipid material, concentration of surfactant and optimization of temperature at preparation of SLNs. The polymorphic kinetic may be depends on the

length of chain. In which the crystallization process is slower for longer chain for the shorter triglyceride chain. The gel is been formed. This may depend on strong beta modification by temperature modification. Various destabilizing factors may affect the SLNs and it may decrease the zeta potential. the drugs are hydrolysed and it has some stability issues. For the long-time stability drying is the most important thing. Some drying techniques are freeze drying, spray drying and lyophilization. For the preparation of SLNs electrospray method. Direct SLN powder are formed. The SLNs formulation are put into capsule, tablets and it has a drug delivery. It may have some restriction for the uncontrol growth by coagulation. It possesses perfect crystal lipid matrices and loaded the drug in between fatty acid chains. For the production and storage of SLNs the enhancement of crystal structure was formed.[45,46]

2. CONCLUSION

Solid lipid nanoparticles, which are colloidal dispersions, have been modified to have the characteristics of other nanoparticles, such as microemulsions, suspensions, liposomes, and polymeric nanoparticles. By gradually avoiding the major issues associated with nanoparticles, SLNs enable the development of a more flexible, chemically stable, and physiologically appropriate drug delivery system. The only issue with them appears to be their propensity to gel, but nanostructured lipid carriers offer a potential solution.[47] Additionally, because of the heat and stress created during synthesis using the hot homogenization method, the active component, or the medicine, may be damaged. So it's important to pick the right production technique. Other issues that need to be addressed include particle size, the coexistence of distinct colloidal forms, diverse morphologies, and drug ejection from the lipid matrix.[48] the numerous tried-and-true techniques for manufacturing the SLN matrix in large quantities. Drugs that are thermolabile, have a low pharmacokinetic profile, or both can be administered to the target site using SLNs. SLNs can also be used to transport proteins and peptides more effectively and with less toxicity. Therefore, the combination of the theragnostic method with SLNs has the potential to change both therapies and diagnostics.[49,50]

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