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(REVIEW ARTICLE)

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Approach of nanostructured lipid carriers (NLCS): tool as a new targeted drug delivery system: A review

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Abstract

The most significant advancement in the creation of more efficient medicine delivery systems has come from nanotechnology. The target drug delivery system is now incredibly simple and efficient thanks to cutting-edge nanotechnology. A target drug delivery system is a technique for getting the medication's active ingredient to the body's injured area. Nanostructured lipid carriers (NLC) are an exceptional and unique development in the field of nanotechnology. Site-specific drug delivery systems can be constructed using NLCs, a novel form of second generation emulsion system that combines spatially incompatible liquid lipids with a mixture of solid lipids. This potential delivery mechanism provides longer stability than SLNs. Because of the potential advantages of drug design at the nanoscale, such as the capacity to increase immunogenicity and bioavailability, which can lead to the development of more convenient administration routes, fewer side effects, improved biodistribution, and an extended drug life cycle, the application of nanostructured and nanophases is seen to bridge the gap between biological and physical sciences.

Keywords: Nanostructured; Nanostructured lipid Carriers (NLCs); Homogenization; Microemulsion; Emulsification

1. Introduction

Based on the nature and composition of lipid, various production technique, and formulation parameters, NLCs is divided into three categories such as;

Type-I: Imperfect NLCs- Formed by mixing of lipids of different chemical properties results in crystal imperfection which shows a high drug payload [1].

Type-II: Amorphous NLCs- A mixture of solid lipids and some special lipids (like isopropyl myristate, hydroxy stearate, hydroxy-octacosenyl, etc.) formed a structure less non-crystalline solid amorphous matrix and results in the expulsion of the drug, minimize the crystallization of lipid matrix, preventing drug repulsion and moderate drug pay-load. The lipid solid state of amorphous NLCs is detected by NMR (Nuclear Magnetic Resonance) and DSC (Differential Scanning Calorimetry) confirming the transition temperature of amorphous NLCs [1,2,].

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Type-III: Oil-in-fat-in-water/multiple NLCs- This type of NLC is composed of nanosized liquid oil compartments which are enclosed by a solid lipid matrix. Due to the nanosized liquid oil compartments, drugs are highly dissolved and act as a barrier to prevent drug leakage, and thereby drug is released in controlled release behavior by increasing drug solubility, drug encapsulation, and drug loading capacity [2]. By using of high concentration of oils, during the hot homogenization procedure a miscibility gap formed between liquid lipid and solid lipid. When these lipids are cooled down, phase separation of an excess liquid lipid occurs and forms a nanosized liquid oil compartment which is surrounded by the SL matrix [3, 4].

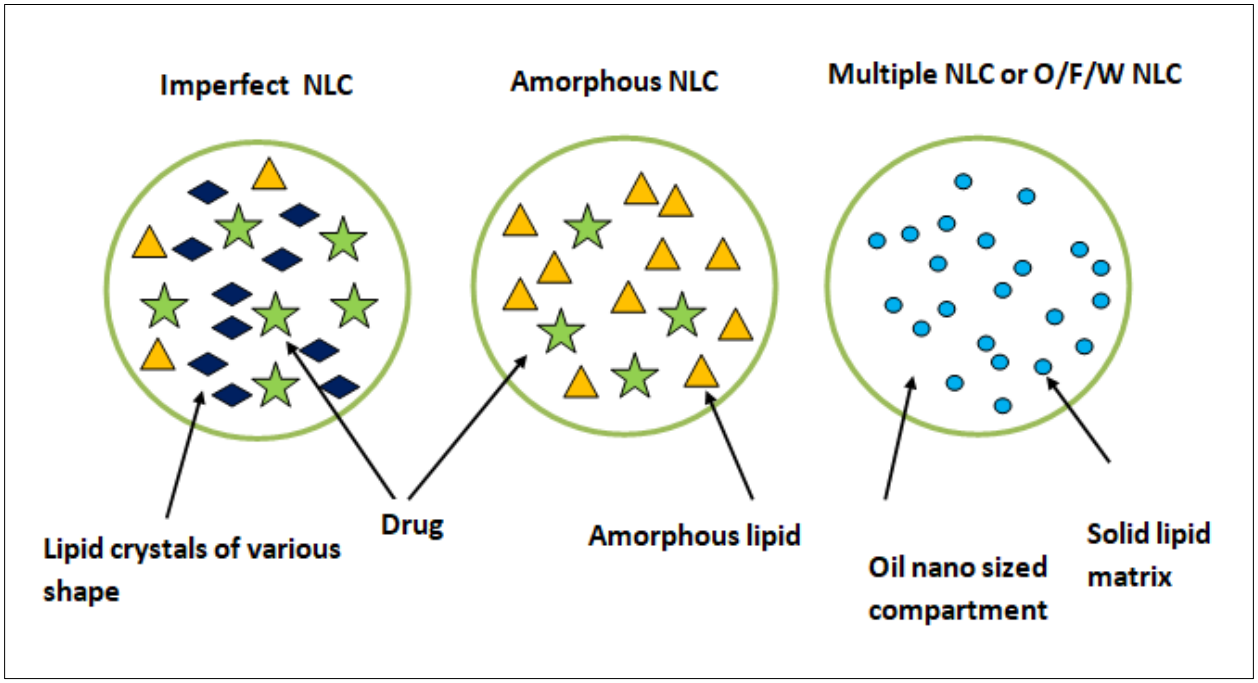

Figure 1 Types of Nanostructured Lipid Carriers (NLCs)

1.1. Methods of preparation

NLCs are the superior drug loading that contains less amounts of surfactants and co-surfactants which control drug release and are less toxic as compared to liposomes. There are various techniques are used in the preparation of NLCs based on energy requirements. Figure 2 enlists different types of techniques used in the preparation of NLC [5].

1.2. High energy required method

This technique is the most widely used method which utilizes both high temperature and high pressure. Here the organic solvents are not used and produce highly stable pharmaceutical nanoparticles, nano emulsions, SLNs, and NLCs under high pressure. Due to the high temperature, the viscosity of the mixture of liquid lipid and solid lipid decreases therefore particle size also reduces. This is more useful for highly lipophilic drugs. Two approaches are used to produce NLCs, which are the hot homogenization and cold homogenization methods [4,6].

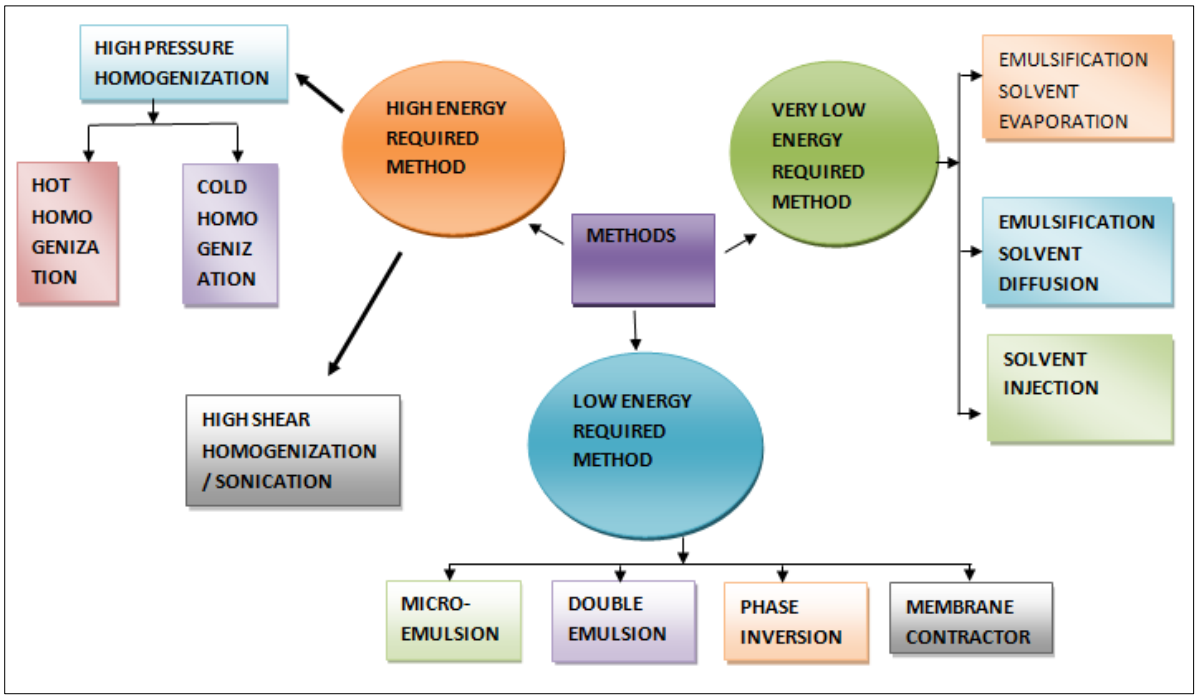

Figure 2 Methods used in preparation of NLC

1.3. Hot homogenization

In this method, the drugs are dissolved in the molten lipids mixture which is homogenously dispersed in hot aqueous solution of surfactant under constant high-speed stirring to produce a hot pre-emulsion. Resultant pre-emulsion is homogenized by high pressure homogenizer like extruder. Further mixing is done by ultra-sonication using water bath sonicator and then NLCs are created by solidifying the mixture by cooling at room temperature [7].

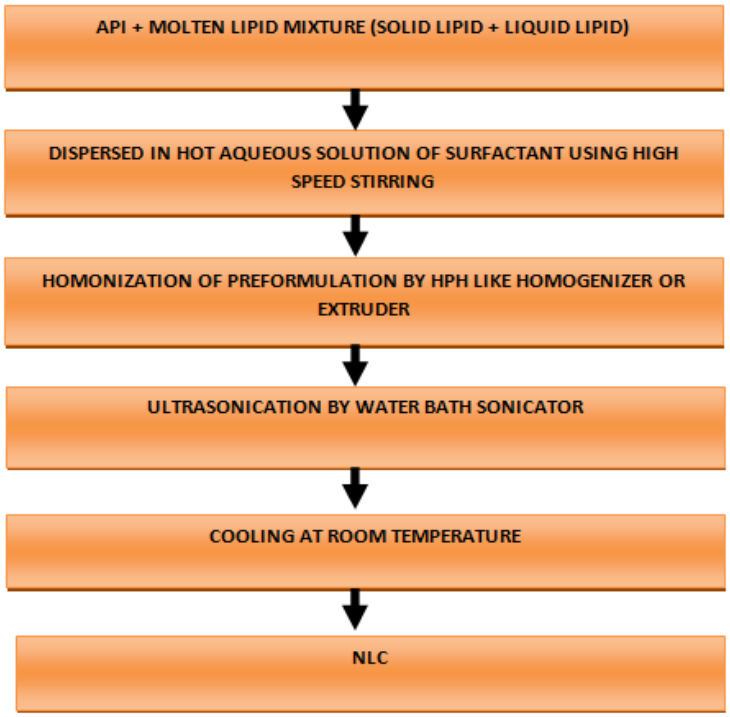

Figure 3 Hot Homogenization Process

1.4. Cold homogenization

During this method, drugs are added to the molten lipid which is solidified by rapid cooling with liquid nitrogen or dry ice. Solidified melted liquid converted to fine micronized particle which is dispersed in cold aqueous surfactant solutions or hydrophilic emulsifier dispersion medium. Resultant dispersion when processed under high pressure homogenizer creates NLCs [8,9].

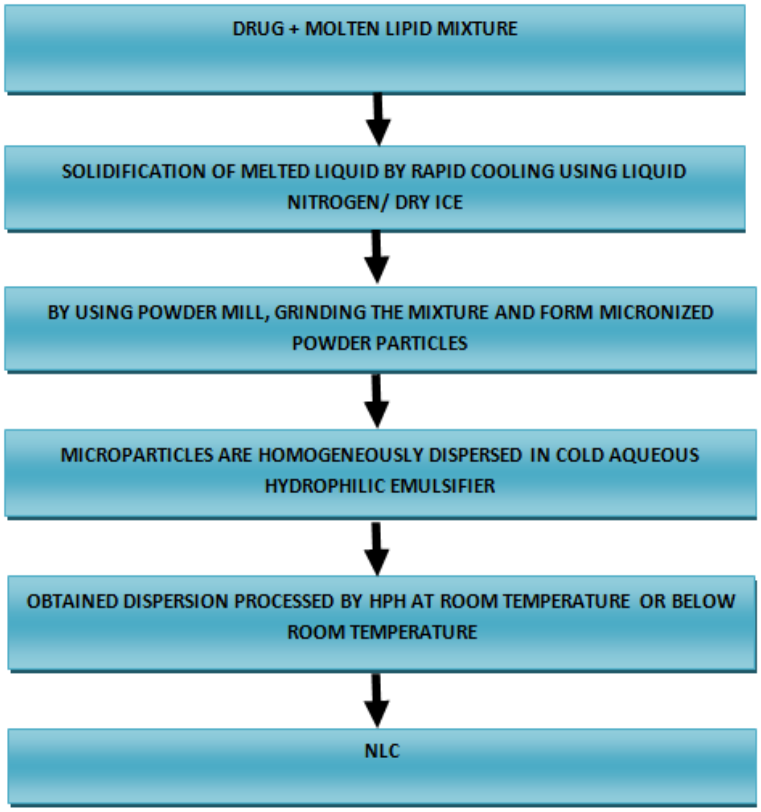

Figure 4 Cold Homogenization Process

1.5. High shear homogenization/ ultrasonication technique

This process involves dispersing or dissolving lipophilic medicines uniformly in a molten mixture of liquid and solid lipids, which is then added to a heated aqueous surfactant media. By mixing at a constant temperature with a stirrer, pre-emulsion is created. The ideal temperature is 5–10 ºC above the solid lipid's melting point. The process of applying a high shear homogenizer yields microemulsion. NLCs are produced when a microemulsion is cooled and solidified [10, 25].

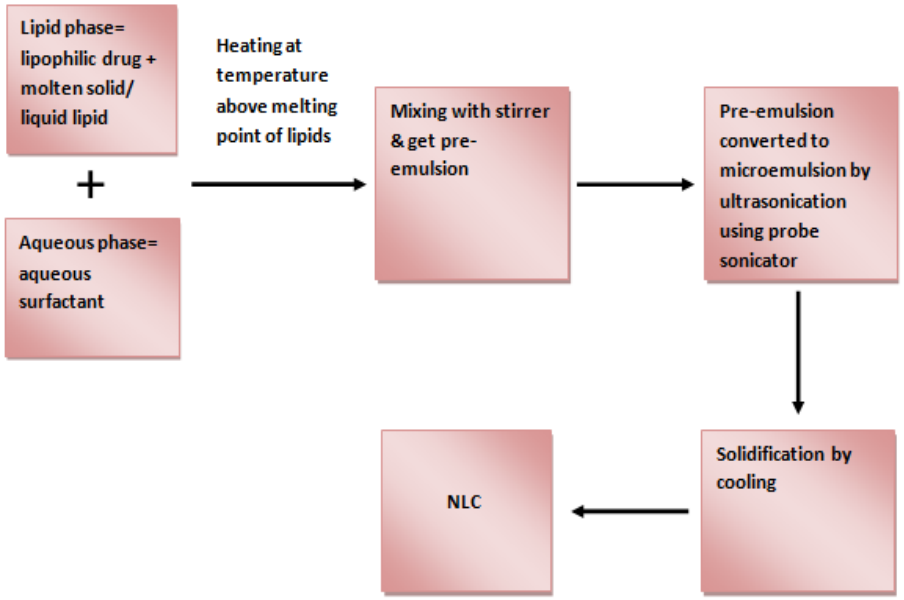

Figure 5 High shear homogenization/ ultrasonication technique

2. Low energy required method

2.1. Microemulsion

Microemulsion is prepared by similar procedure of ultrasonication technique. By using probe sonicator micro emulsion is formed which is dispersed in cold water to get nano-emulsion. Finally, NLC is created by recrystallization of Nano emulsion [11, 12].

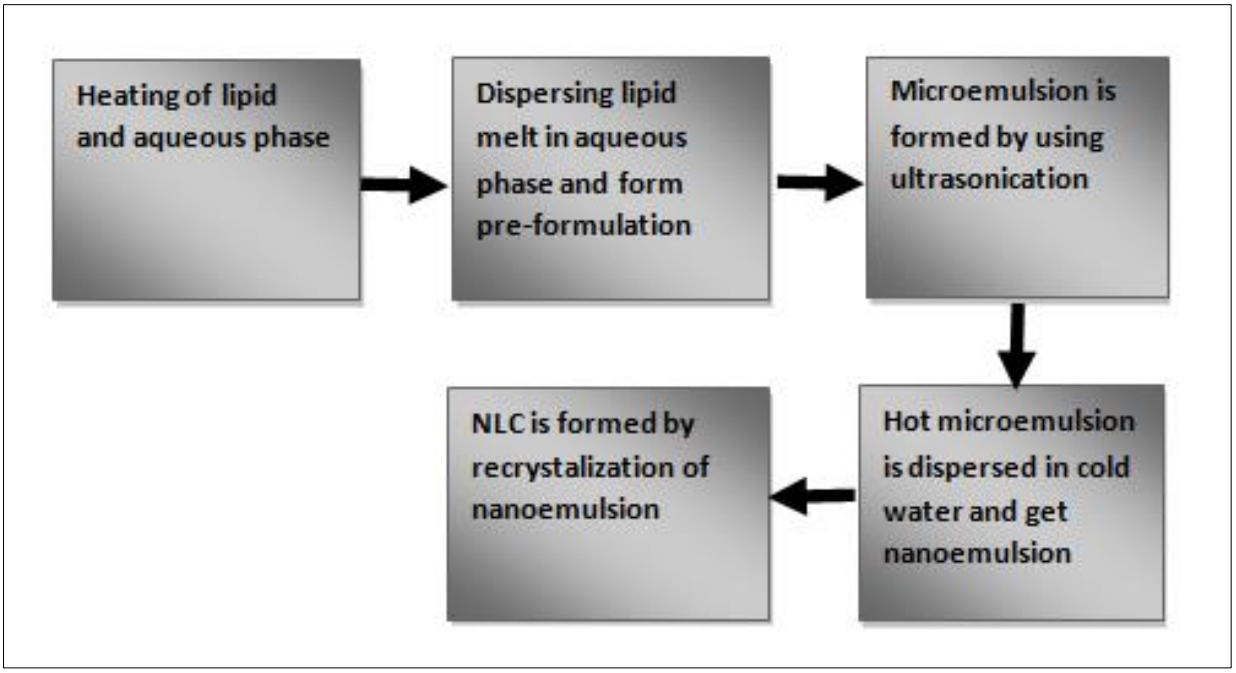

Figure 6 Microemulsion Process

2.2. Double emulsion

Aqueous phase containing drug solution which is dispersed in lipid melts by heating and form primary emulsion W/O. This W/O emulsion further dispersed in secondary aqueous medium and forms W/O/W which is precipitated by cooling and results in NLCs [13, 24].

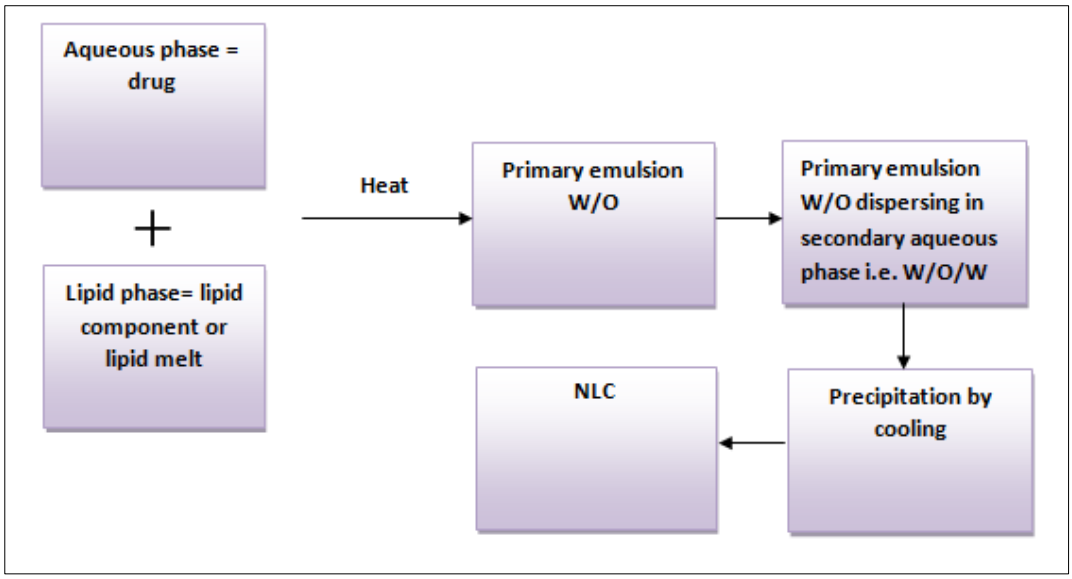

Figure 7 Double emulsion Process

2.3. Phase inversion temperature

In this technique, lipid melt is dispersed in an aqueous phase i.e. O/W emulsion is obtained. O/W emulsion is heated up to 85ºC and forms the W/O phase which is then cooled at a temperature up to 60ºC to get the O/W phase. This procedure is repeated to three heating and cooling cycles to get a phase inversion zone. Then NLC is formed by dilution of O/W emulsion with water [14]

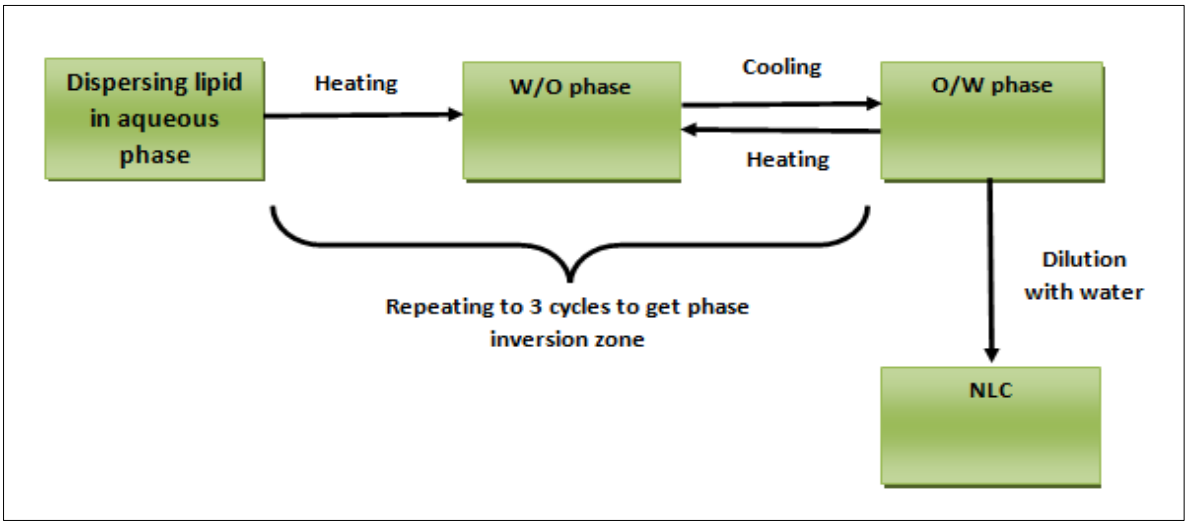

Figure 8 Phase Inversion Technique

2.4. Membrane contractor technique

When they are pushed up against the porous membrane, tiny lipid droplets are removed from the pore and lipid melts disseminate across the membrane module. NLCs are produced once the lipid droplets are cooled to room temperature [15, 22].

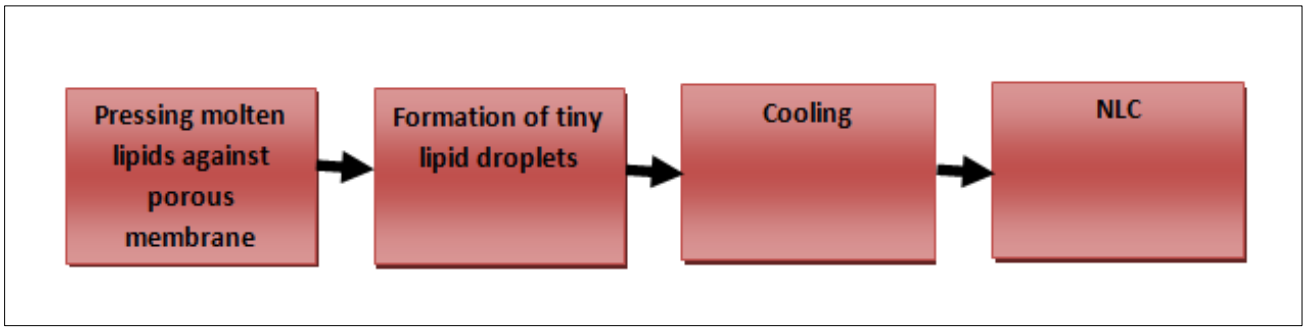

Figure 9 Very low energy required method

2.5. Emulsification solvent evaporation

Drug and molten lipid mixture is dissolved in a water immiscible organic solvent. The obtained organic solution is added to an aqueous surfactant solution which is emulsified by ultrasonication or high shear homogenization. NLC is obtained by evaporation of organic solvent under reduced pressure [16].

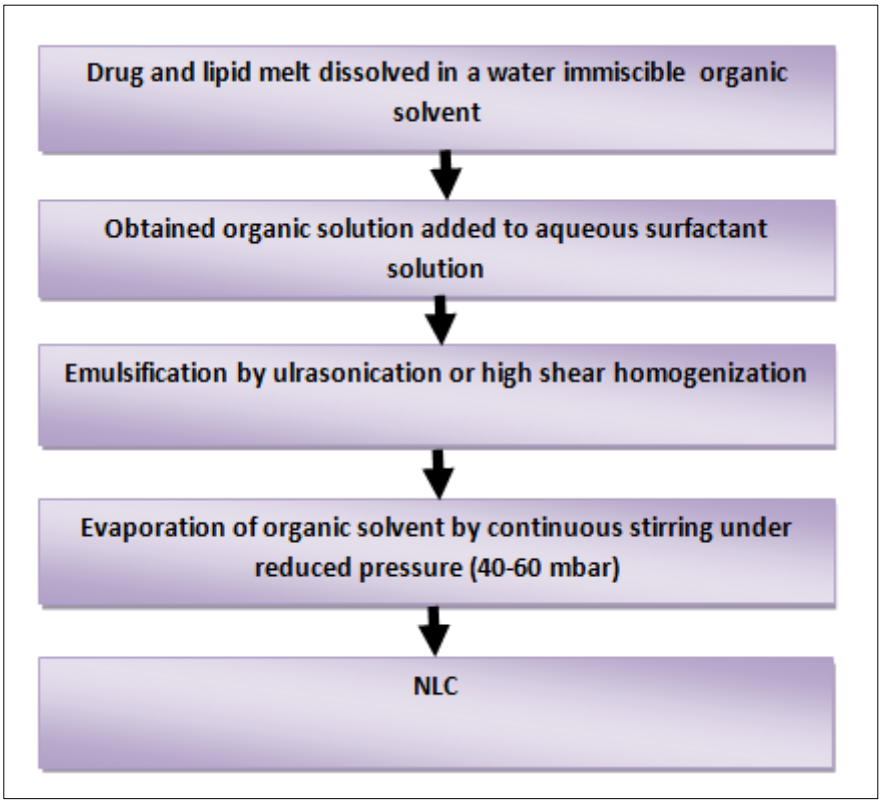

Figure 10 Solvent evaporation Process

2.6. Emulsification solvent diffusion

Drug and lipid melt mixture is dissolved in a water-miscible solvent. The resultant solution is added to an aqueous surfactant to achieve thermodynamic equilibrium. Obtaining O/W emulsion is then added to water and stirred followed by applying high pressure homogenization until diffusion of organic solvent and solidifies the dispersed phase to get NLCs [18,19, 20].

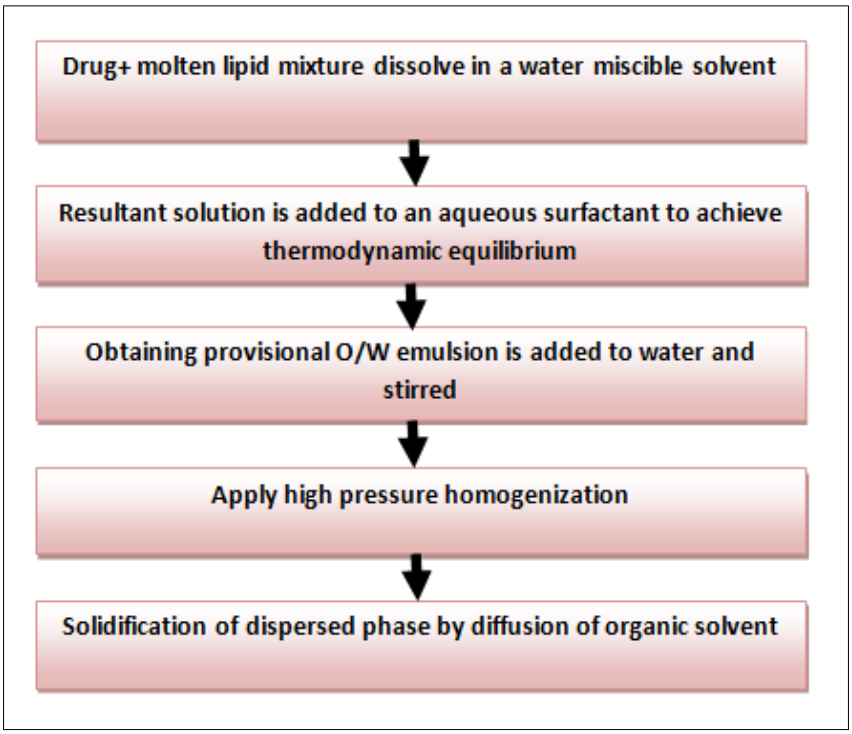

Figure 11 Solvent Diffusion Process

2.7. Solvent injection

Active substance and lipid melt mixture is dissolved in an organic solvent which is injected into aqueous surfactant solution under continuous stirring followed by sonication with probe sonicator and get NLCs [18].

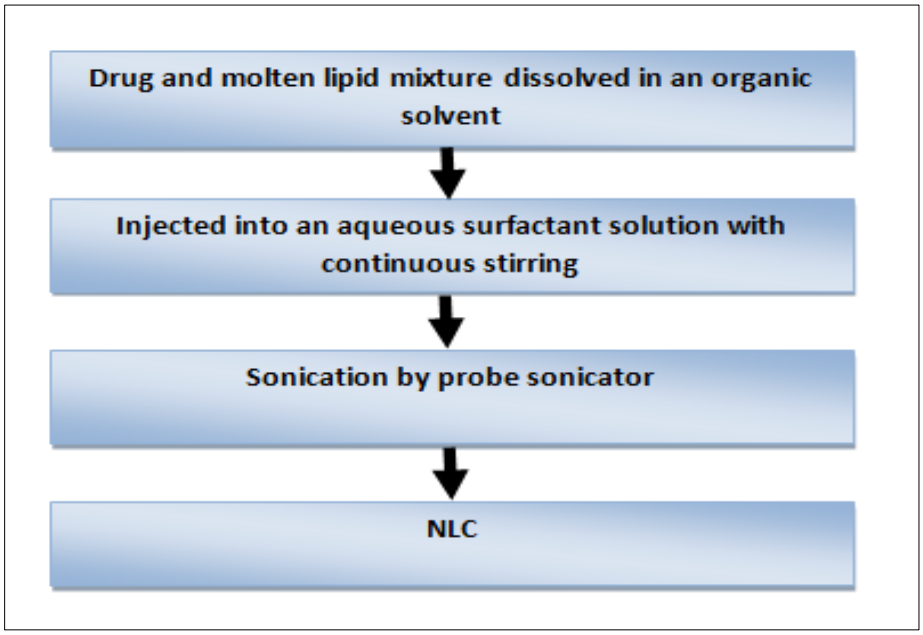

Figure 12 Solvent Injection Process

3. Conclusion

NLCs have the potential to be a successful enteral medication delivery technology. Because of their lipid nature, NLCs offer Page | 70 special properties that help them overcome the drawbacks of oral administration. These include protection against pH and enzyme activity, improved absorption from the gastrointestinal tract through intestinal

lymphatic system transportation, and improved biocompatibility and bioavailability of drugs. Without a doubt, NLCs also have the advantages of nanomaterials, including a flexible system that can be used for hydrophobic chemical encapsulation and the ability to hold reasonable hydro-phylic chemicals through the use of hydrophobic ion pairing process or polymer blending. NLCs include a variety of bioactive substances, either as single or several compounds, for oral use in therapeutic applications. While systematic delivery could deliver therapeutic agents to the targeted organs, such as the brain, liver, and kidney, as well as cancer tumors, it could also improve drug bioavailability for the treatment of malaria, anaphylactic shock, hypertension, and other conditions. Site-specific NLCs are used for the primary treatment of gastric and colon diaeases. Studies have shown that oral NLCs would perform even better in a range of applications, particularly for chronic disorders, with the support of more sophisticated technology in fabrication and evaluation for industrial concern.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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