Lipid nano-emulsion for the treatment for breast cancer

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Abstract

LNEs are being extensively researched as drug carriers along with additional nanocarriers for better drug delivery, especially when used for chemotherapeutics. They have the potential to cure breast cancer and other types of tumours by binding to receptor domains where LDLP-receptors are overexpressed. LNEs are oil-water dispersions with the nanoscale droplets stabilised by a surface-active layer where they mitigate the creaming and sedimentation throughout storage and coalescence, resulting in an even greater oil-in-water vicinity. The oil phase of the systems promotes lipophilic solubility of drugs, resulting in reduced dosing volume, preserving them from the bloodstream and tissues, with mitigating the pharmacokinetic imbalances. In contrast to other conventional formulations, these innovative nanocarriers offer the ability to incorporate poorly water-soluble drugs and exhibit sustained release, selective distribution, and reduced drug toxicity. LNEs are capable of being processed into a range of compositions and are safer to use, biodegradable, and biocompatible. There are a number of techniques to prepare LNE for parenteral used in which high energy emulsification is most frequently used. A comprehensive description of LNE, including the basic components, benefits, preparation techniques, characterisation, conceivable uses, and present research trends, will form the primary thrust of this review.

Keywords: Lipid nano emulsion, Nanocarrier, Bioavailability, Chemotherapeutics.

1. Introduction

Over 60 % of novel APIs are reported as poorly water soluble with the advancement of more sophisticated drug discovery which makes significantly diminished activity of these drugs despite having potent pharmacological activity [1, 2] . These drugs are too difficult to administer through a vein, hence an adequate delivery carrier must be used. Lipid based nanoparticles (LNPs) have gained a lot of interest due to their exceptional pharmacological activity with favourable therapeutic outcomes [3, 4]. Lipid nano emulsion (LNE) is one of innovative nanocarrier (NC) falls under LNPs has been gaining a rising attention due to its diverse characteristics such as the ability to incorporate poorly aqueous soluble drug and their biocompatibility [1]. The LNE is a promising drug delivery vehicle due to its sustained release, tailored distribution, and low drug toxicity [5]. They are able to enhance the drug release after injecting the chemotherapeutics intramuscular and intratumorally with the improved transport through the lymphatic system [6].

Chemotherapy nevertheless remains a recommended therapeutic alternative in clinics for breast cancer, the most common cancer in women with significant mortality and morbidity [7]. However, the main constraints limiting the therapeutic applications of chemotherapy includes their adverse effects such as damage of healthy tissue and emergence of drug resistance [8, 9]. LNEs are therefore revolutionary in the treatment of breast cancer and other types of tumour in order to alleviate these concerns, such as their efficacy and biosafety [10]. Considering the cancerous targeting cells, LNE binds that receptor domains where LDLP-receptors are overexpressed, accumulating chemotherapeutics leads to reduce the toxicity [11]. The theoretical concept behind the parenterally administrating LNE is that the formulations injected with triglycerides to seriously affecting patients who are unable to feed orally, where the IV-fat get metabolized into essential fatty acids by releasing the therapeutics [12]. LNE may relieve pain from IV-injection by exposing tissues to lower doses or avoiding tissue-irritating carriers in order to culminating with greater patient compliance [13].

LNEs are heterogeneous mixture of two immiscible liquids (o/w or w/o) in which one component is dispersed in another as depicted in **Fig 1**. The physical stability of formulation often could be improved using suitable emulsifiers that forms a coating film around droplet reducing interfacial tension through increasing the droplet-droplet communication [3]. LNE is an opportunistic nanoparticulate system primarily consisting of liposomes and single or double emulsion [4]. To prepare the LNE avoiding hydrolysis of poorly aqueous soluble drugs before reaching the targeted site, drugs are frequently incorporated within the oil matrix or oil-water component, which are the interior phase and interface of the system [14].

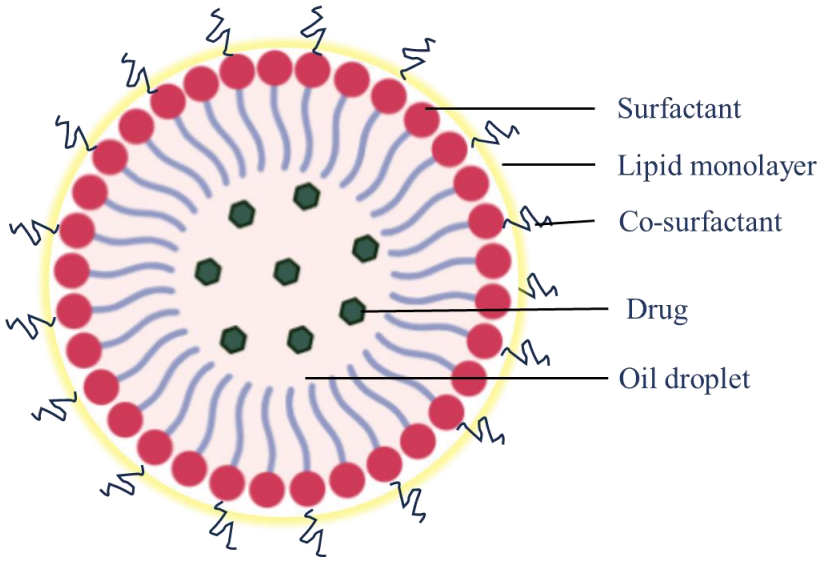


Fig 1: Schematic representation of structural configuration of drug loaded lipid nano emulsion

1.1 Advantages of LNE over other conventional formulations [4, 6, 9, 15]

- Formulated through uncomplicated techniques.
- Comprised of biodegradable materials such as vitamins and essential oils.
- Biocompatibility within excipients and tissue environment.
- Carrier system releases the drug with avoidance of burst effect.
- Able to transport efficiently at targeted site owing to their more surface area and free energy. The immense surface area of LNE facilitates the efficient movement of API through semipermeable membranes too.
- Capable of being processed into a range of composition such as liquid injectables, foams and creams.
- Holds a remarkable kinetic stability.
- Possess significant amount of drug loading in their core.
- Comprises surfactants that are mostly considered as safe for human usage.

1.2 Limitations of LNE [16]

- The fluidity of material in liquid media offers challenge for the optimum surface alteration of the particle.
- The short-coming in drug loading may occur for high dosage drug regimens although having appropriate oil solubility since there are limiting oil components (NMT 30%) are designed to prevent systemic irritation.
- Delays in plasma clearance in susceptible individuals with fragile nano-emulsion infusions may be due to potential embolic fat globules and safety concerns with injections [17].

2. Suitable candidates for formulation of LNE and their types

As stated earlier, the LNE are oil-water dispersions with nanoscale droplets stabilised by a surface-active agent, majorly composed of oil phase (MCTs), phospholipid (DOPE/DOPC), surfactant, soy or egg-lecithin and water where the formulation constituents are generally recommended as safe (GRASS) status [6]. **Fig 2** represents the structural composition of a variety of components used in preparation of LNE. By virtue of their nanosized droplets, they offer a significantly larger oil-in-water contact area than conventional emulsions, which improves drugs release [18].

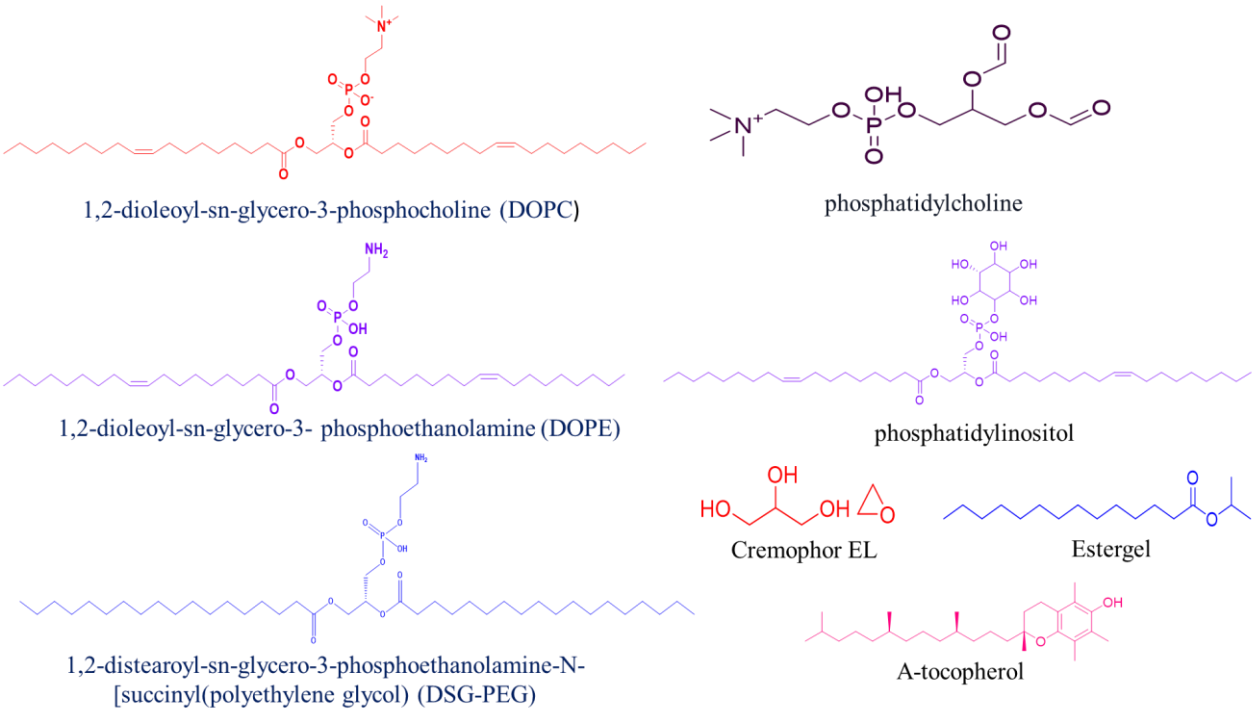


Fig 2. Chemical structure of a variety of components used in preparation of LNE

The oil phase in LNE system could serve as a potent solubilizer for the lipophilic moiety resulting the lipophilicity of drug greatly enhanced which further reduce the dosing volume compared to an aqueous system [19]. Masahito et al formulated the LNE by providing hydrophilic moiety to surface of NE to ensure the prolonged circulation in blood composed mainly of soyabean oil, water, lecithin, glycerol and HEPC in a specified ratio [20]. Other lipidic components include the stearic acid, isopropyl myristate, cetyl palmitate, and α-tocopherol [21]. Surfactants are the compounds with amphiphilic characteristics which lowers the interfacial tension by inhibiting the droplet aggregation enabling the stability to LNE. Since, having an efficient immobilization at oil-water interface, they additionally provide the dual stability such as electrostatic and steric (electro steric). Perhaps the most frequently employed surfactant in LNE is phosphatidylcholine due to less prone to degradation [22], which is

derived from egg yolk or soybean while others are the Cremophor EL (Polyoxyl-35 castor oil) and bile salts (sodium deoxycholate) etc. The surfactants used in preparation of LNE could be either ionic, non-ionic or zwitterionic [19, 23]. Emulsifying agents are primarily used to mitigate droplet fragmentation by top-down approaches in order to reduce droplet size while eliminating aggregation, sustaining stability of LNE over a longer time frame [24]. A key factor in the emulsification of LNE is the type of oil-emulsifier ratio, the emulsifier's concentration and ratio, and other factors such the temperature at which the excipients are selected collectively.

Based on their composition and structure, LNEs can be separated into a wide range of types. First-generation lipid nanoparticles, known as solid lipid nanoparticles (SLNs), comprised of a surfactant shell and a solid lipid core. Solid and liquid lipids are combined in order to develop a more complex structure with enhanced stability and drug loading capability in nanostructured lipid carriers (NLCs). Both hydrophilic and hydrophobic drugs reside in phospholipid bilayers found in sphere-shaped vesicles called liposomes. Lipid Polymer Hybrid Nanoparticles are suited for gene delivery because they combine polymers and lipid-based components [25, 26].

3. Method of preparations

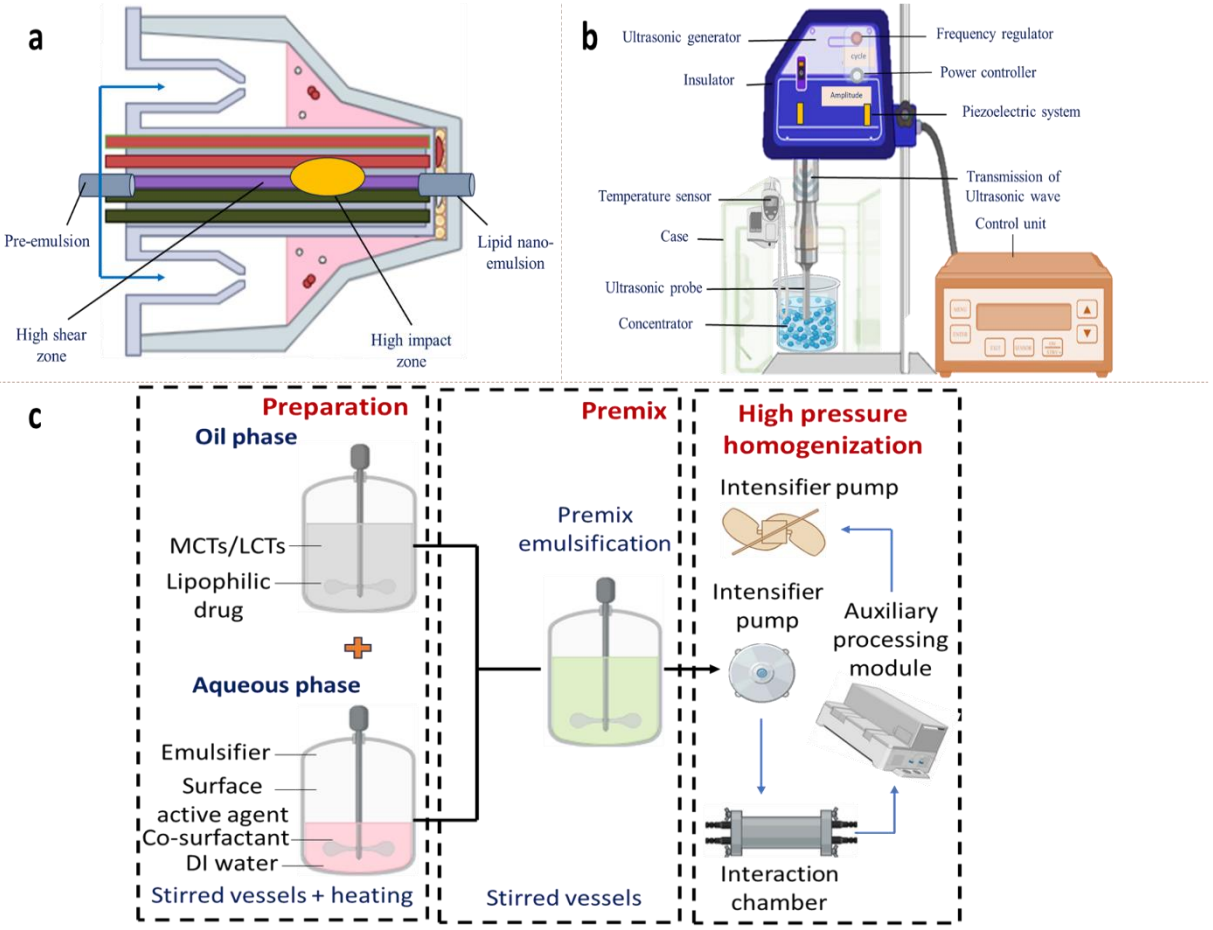
A variety of methods of preparations are there to prepare LNE where it mainly focuses on the high-energy emulsification (HEE) and low-energy emulsification (LEE). The HEE involves a mechanical device, while the LEE relies on the chemical potential of the surfactant constituents. Micro fluidization, ultrasonication, and high-pressure homogenization (HPH) are some of the offered strategies of HEE depicted in **Fig 3**. while the LEE treatments encompass the phase inversion temperature (PIT), phase inversion composition (PIC), premix membrane emulsification (PME), and solvent diffusion [27].

3.1 Micro fluidization

The technique of micro fluidization involves compelling a fluidic mixture (lipids) into an interaction chamber with extreme pressure, resulting streams splitter into halves followed by integrating these at extremely high velocities [28]. This process produces nanosized or submicron LNE that have a small size distribution due to its strong shear, turbulence, and

cavitation effect [29]. Most frequently, there is a device called Microfluidics having the Laminar extension flow which is deemed to be behind droplet disruption at the chamber's inlet.

Fig 3: Flow diagram of the HEE approaches to prepare LNE a). Micro fluidization b). Ultrasonication c). High pressure homogenization.



3.2 Ultrasonication

An effective method to decrease mean droplet size in preparation of LNE for small trial batches is ultrasonication. There are three essential parameters such as power, frequency, and duration of ultrasonication that affects the emulsification process. The ultrasonic vibrations create crushing and tensile strains causing acoustic cavitation and abrupt bubble collapse to mitigate the size issue [30]. The acoustic pressure and acoustic streaming along with cavitation produced by ultrasonic emulsification refers to high pressure-high temperature waves [31]. Sound energy generated by the piezoelectric probe causes cavitation bubbles to rise erratically until they disintegrate and reduce in size [32].

3.3 High pressure homogenization (HPH)

Being a HEE, the HPH method is advantageous having a stable system, uniform and small particle size distribution, rapid emulsification time with lower surfactant demand. The emulsifier and oil phase are mixed with surface active agents and cholesterol evenly followed by stirring. Then DI water and dispersed phase are mixed to obtain a crude emulsion which undergone homogenization with subsequent cooling and adjusted to neutral pH 7 [33]. The HPH produces injectable LNE differently than other methods in order comply with USP standards for microbial attributes and droplet size. It consists of three main steps: preparing water and oil phases, emulsifying oil and water phases into a coarse pre-emulsion, and converting the premix into a final LNE where every step is carried out in a nitrogen environment to prevent oxidation of lecithin and PFAs [34].

3.4 Modified thin film hydration

A frequently used preparation technique for LNE is thin film hydration shown in **Fig 4**, which entails dissolving the lipid ingredient in a volatile solvent, producing a thin film, followed by hydrating the film with an aqueous solution. This process may outcome in heterogeneous LNE and distinct structural organisation, however in order to control physicochemical characteristics and reduce their droplet size, additional steps such as sonication, membrane extrusion, and HPH are required. However, this strategy is challenging, and there are limitations such as poor encapsulation efficiency, unpredictable functioning, and scaling concerns [35, 36].

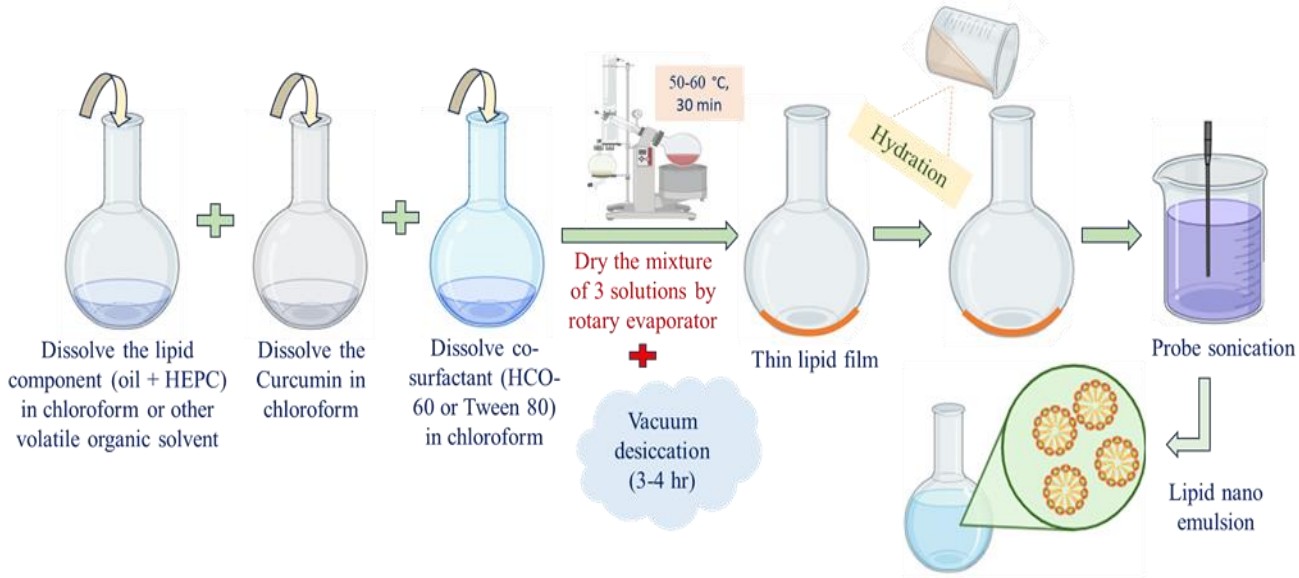


Fig 4: A modified thin film hydration technique for the preparation of LNE [37].

The LNE was prepared earlier by using this technique to incorporate Curcumin where the oil phase, water, phosphatidylcholine and surfactant were dissolved in appropriate organic phase such as chloroform and dried the mixture using rotary evaporator subsequently followed by vacuum desiccation to get thin film. Then the film was hydrated using aqueous phase and subjected to sonication for 5 to 10 minutes to obtain the fine lipid nano emulsion [38].

3.5 Phase inversion temperature (PIT)

The PIT method has grown in acceptance over high-energy emulsification since it can produce homogenous and smaller droplets without making use of expensive machinery [39]. Temperature has an enormous impact on the spontaneous deformation of temperature-sensitive surfactants, with low temperatures producing positive curvature and high temperatures producing negative curvature. Surfactants have the same affinity for both aqueous and oil phases at an intermediate temperature, avoiding spontaneous curvature and total oil the solubilization in a lamellar liquid crystalline phase [40, 41]. The ultra-low oil-water interfacial tension at PIT is ideal for nanometre-sized droplets.

3.6 Solvent diffusion

The fatty acid, oil phase, and surface-active agent are dissolved in mixture of organic solvent and heated below the boiling temperature. Then, it gently dispersed in DI water with constant stirring for 5 to 10 minutes at rpm up to 500. The resulting mixture was then centrifuged, exposed to acidic precipitation, and the retrieved precipitate was repeatedly washed and redispersed in DI water [14]. The approach involving emulsifying a water-miscible organic solvent in an aqueous phase and dissolving the lipid matrix has been described in an article published by Trotta and colleagues. Depending on the oil-emulsifier ratio, the lipid precipitates in the aqueous media as the solvent evaporates at reduced pressures, generating a dispersion of LNE with droplets smaller than 100 nm. Controlling the amount of heat produced is an essential advantage of this approach [42].

3.7 Premix membrane emulsification (PME)

In the past decade, PME has grown into a viable alternative to the manufacturing of LNE for parenteral administration. This technique produces droplets with diameters in the nanometre range by continuously extruding a coarse pre-emulsion through a nano-porous membrane, generating comparatively little heat at pressures beneath 60 bar [43]. The materials which

are thermolabile or susceptible to shear stress, a low energy input could prove advantageous. Furthermore, PME can be used to produce LNE at very small volumes (0.5 mL) which is significant in formulating novel formulations for expensive or highly potent drugs. On the other hand, PME can produce extremely narrow particle size distributions [44, 45].

4. The ideal characteristics of LNE and their determining techniques

The LNE should have some characteristics for better drug loading and release pattern especially for injectable purposes. The prepared formulation most often subjected to their size and, PDI for optimization purposes followed by morphological evaluation. Some of the techniques and their determining techniques are described in preceding section.

4.1 Particle size and PDI

The size, shape, surface charge and the entrapment efficiency are some critical features that must be established prior to exploring the LNEs and their synthesizing approaches. The size is important characteristics which affect the stability, biodistribution, cellular absorption and overall therapeutic efficacy of system [46]. Sizes larger than 100 nm might display higher drug loading but lower cellular absorption, according to reports. However, size smaller than 100 nm tends to show better cellular absorption with longer circulation time [26].

The particle size and PDI of LNE are often detected using dynamic light scattering (DLS) and single particle optical sensing (SPOS), where the particle size is typically expressed by the Gaussian width of distribution or mean hydrodynamic diameter. The LNE is diluted two thousand times with water for the same reason [47]. The size distribution and mean particle size are important variables when developing injectable formulations of LNE. Since the ideal size range for systemic drug absorption via IV injection is between 50 and 150 nm, LNE typically have an average particle size of 100–400 nm [48]. The PDI, ranging from 0 to 1, indicates the degree of dispersion of particle size. A value of PDI of below 0.2 usually signifies a narrow size distribution, while nearly all studies attribute a threshold of PDI 0.3 or lower [49].

4.2 Surface morphology

The surface morphology and properties of LNE could be accessed through the techniques such as scanning microscopy (SEM), transmission microscopy (TEM) and atomic force microscopy

(AFM). In physiological environment, LNEs show promising advantages in being well defined smooth surface characteristics where it reduces the possibility of opsonization. The rough and irregular surface could lead to uneven biodistribution arises from unwanted interaction, hence overall reduction in therapeutic outcome.[50]

4.3 Zeta potential (ZP)

The degree of repulsive force is measured using ZP to show how stable the LNEs are. Through a strong repulsion, the aggregation of nano-sized emulsion could be prevented. Most frequently, the ZP value lies in range of ±30 mV has been believed to repel each other concurrently and maintain electrostatic stability. The LNE containing non-ionic surfactants usually having lower ZP values [51]. Furthermore, it has been determined that the ZP value of LNE increases with increasing percentage of oil component. On the contrary hand, neutral charge is ideal for systematic drug distribution [52] while positively charged globules are believed to interact with negatively charged cell surfaces more efficiently [53].

4.4 Stability study

Stability studies refers to the ability of LNE to maintain their physical and chemical integrity, such as size, shape, and lipid legitimacy, over a long period of time throughout a range of environments [54]. Stability of LNE on storage condition is one of the important characterization tests where the undiluted formulations are kept at two independent temperatures at - 4 °C and 20 °C and observed for no visible phase separation. The lack of any obvious change in pH, drug content, and droplet size implied that the instability of phenomenon that often influences the LNE [55].

4.5 Efficacy of phase distribution

The drug distribution in LNE is evaluated by ultracentrifuging the formulation at nearly 2000 rpm for a period of time and separating it into different phases of oil, phospholipids, and water. For HPLC or other spectroscopic analysis, the oil phase is diluted with isopropanol, and the aqueous phase is filtered. The total PTX content in LNE was separated to get the PTX content in the phospholipid layer [56].

4.6 Safety assessment of IV injection

The LNE formulation is injected at tumour site of subject, hence the assessment of safety concerns on injection becomes essential. The investigation of IV-irritation, haemolytic test and acute toxicity are generally performed regarding the above mentioned study [1]. Two rabbits are injected with LNE daily for three days, with saline serving as a control. After sacrifice, the vascular tissue is analysed histopathologically for irritation evaluation. The fibrinogen is extracted from rabbit blood and erythrocytes are washed with 5% glucose, mixed into a 2% LNE and incubated at 37°C for three hours before cooling to 0°C for five minutes to perform the haemolytic study [57]. Mice treated with the LNE formulation and the marketed one are divided into distinct groups for the acute cytotoxicity testing, and the Bliss method is used to determine the LD50 value [58].

4.7 Encapsulation efficiency (EE)

Considering a greater EE is preferred for achieving a uniform distribution of drug, it is crucial in determining the EE in order to estimate the percentage of drugs that are efficiently entrapped in nano-carriers. The %EE can be determined through direct and indirect method where the supernatant is collected in later one. The %EE is estimated using the following formula.

$$\%\, EE = \frac{\text{encapsulated amount of drug by lipid nanoemulsion}}{\text{Total amount of drug}} \times 100$$

There are some key parameters that affect the EE of LNE such as the nature of drug, crystallinity and their solubility in organic and aqueous phases [59, 60].

4.8 Drug-release profiles

Generally, biodegradation and diffusion are the two processes that control almost all of drug release from LNPs. In-vitro drug release is quite helpful to estimate how drug-loaded LNE behave in vivo. The *in-vitro* drug release study of LNE is performed generally using the dissolution apparatus having rotating basket method. The LNE (0.1 mg) was placed in a dialysis bag, plugged at both ends, and immersed in 250–500 ml of dissolution fluid containing 0.5% surfactant, while maintaining the basket's rotation speed at 100 rpm and the bath temperature at 37 °C. Five millilitres of samples are pipetted at predetermined intervals, followed by replenishment by fresh media. Using a 0.45 µ filter, the samples are analysed using an appropriate spectroscopic technique [61, 62].

5. Emerging trends and case studies of LNEs

Increasing drug bioavailability and specificity while removing off-target effects is the primary objective of LNE, a new NC that is quickly becoming renowned for creating effective therapies for cancer [15]. They are potentially useful nanoparticulate systems for encapsulating and delivering large concentrations of lipophilic substances for biocompatible therapeutic purposes. A number of studies already proven the efficacy of LNE for tumour targeting especially in breast cancer out of which few are described here [4]. Jiang et al. reported an investigation using a solvent-diffusion approach for DOX-loaded LNEs (DOX/LNE) and PEG-modified LNEs (DOX/PEG/LNE). MCT, soybean oil, lecithin, DSPE-PEG, and DOX were dissolved in a DMSO and ethanol mixture as a component to the process being performed. The process involved dissolving MCT, soybean oil, lecithin, 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N- [carboxy (polyethylene Glycol) (DSPE-PEG), and DOX in a mixture of DMSO and ethanol followed by the solution was heated, dispersed in DI water, and adjusted to a pH 1.2. Then the LNE precipitate was centrifuged, redispersed, and washed twice with DI water and observed that the obtained formulation had a size below 50 nm with satisfactory stabilization up to 3 months and better cellular uptake [14].

Chen et al developed The LNE of PTX for tumour delivery, which entailed combining MCT-LCT (1:1) and oleic acid as an oil phase, followed by glycerol, surfactant, and distilled water as an aqueous phase. The oil phase was progressively added to the aqueous phase, producing a coarse emulsion. The emulsion was homogenised, yielding 10% blank LNE with particle sizes of 220nm to 380 nm and observed a higher drug loading with longer drug release of PTX in the oil phase. Additionally, the drug showed larger plasma AUC_0^{∞} value, a smaller plasma clearance (CL), and a longer mean residence time (MRT) with a significant decrease in extraction by RES organs, an increase in tumour uptake, stronger cytotoxicity against MCF-7 cells, and more potent anticancer efficacy on MCF-7 tumour-bearing nude mice [1].

Zhang et al. employed approved ingredients and a procedure of scale-up production to create an LNE with the chemotherapeutic drug DOX. An ionic combination with oleic acid (DOX-OA) was designed to increase the lipophilicity of DOX, resulting in an increase in entrapment efficacy from 30% to over 90%. The DOX-OA LNE was formed by a vortex and rehydrating the lipidic film. A pharmacokinetic analysis revealed lower cardiac contents with greater AUC and circulation time in blood compared to DOX solution. In the contrary to PEGylated liposomes, the release pattern was biphasic and had a shorter circulating time frame [12, 63].

Li and co investigated the anti-tumor activity of PTX/DHA-FA-LNEs against breast cancer in both vitro and in vivo. Using MCF-7 cell lines, the LNE elicited dose-dependent cytotoxicity, enhanced apoptosis, and consistent release of PTX and DHA. The targeted action has been assisted by FA receptor-mediated endocytosis, and PTX/DHA-FA-LNEs substantially inhibited the growth of tumour volume with increased survival time and decreased toxicity [64]. In another study, it is found that patients with breast cancer were introduced LNE within the lesions of tumour 12 hours prior to surgery composed of probably by the 47.8% phospholipids, 48.0% cholesteryl oleate, 1.9% pure cholesterol and 2.3% of triaglycerols. It was also observed that the strong peritumoral effect using the ^{14}C-labelling to cholesteryl oleate [65]. The trends to prepare LNE is growing day by day and potential to target other type of tumours could be explored in future.

6. Biomedical application

LNEs, which are predominantly natural lipid droplets anchored by phospholipids, have applications in therapeutics to provide nutrients intravenously as well as to transport anaesthetics and cancer therapies depicted in **Fig 5**. They also serve in the pharmaceutical, cosmetic, and food industries, with examples being homogenised milk and plant-based milk products [66].

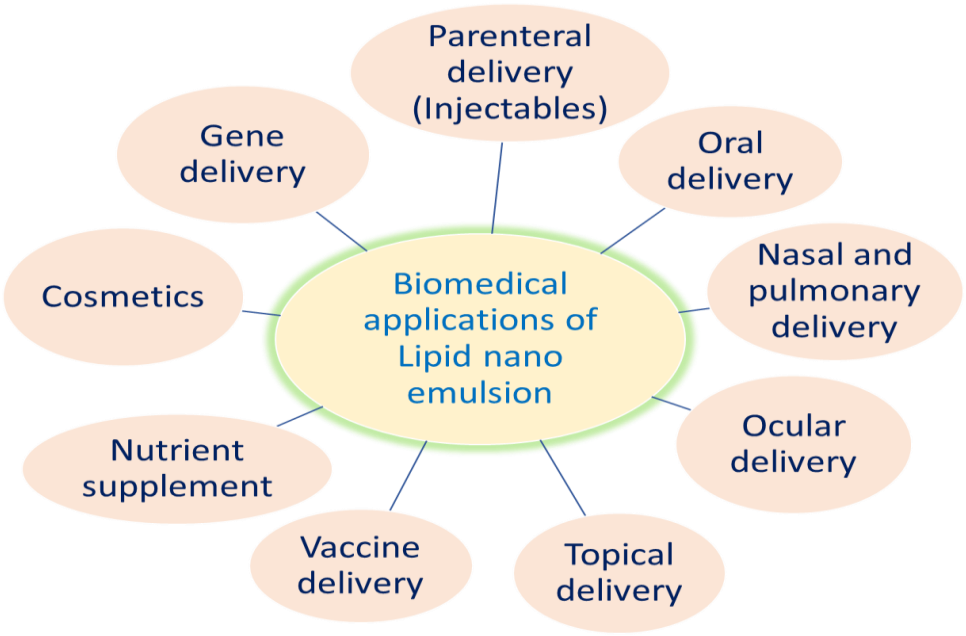


Fig 5: Therapeutic application of LNE for various purposes

6.1 LNE for parenteral use

Parenteral LNE is used to administer drugs with low bioavailability or minor therapeutic aspects and can easily enters the body's biological membrane considering it's lipidic nature. An anticancer drug Chlorambucil which is lipophilic in nature formulated as LNE to treat breast and ovarian cancer [67]. In another study Tagne et al. developed the LNE to improve the efficacy formulation against breast cancer. Further research is required to develop a colon cancer model that would decrease tumours far better than conventional prescribed drugs. The total anticancer efficacy was significantly increased by a stably modified Vit-E LNE of PTX [68].

6.2 Ocular delivery of LNE

In an attempt to deliver drugs that are poorly retained, unstable with water, environmentally sensitive, or poorly absorbed (by the trans corneal route), LNE has been administered via the ocular route. Transparency, viscosity, and refractive index are all given particular consideration whilst producing NEs for ocular delivery. Hagigit et al. used a cationic NE made of DOTAP to improve the dispersion of ocular formulation in an effort to relieve retinal neovascularization [69].

6.3 Pulmonary delivery of LNE

Amphotericin B is capable of being distributed directly into the lungs owing to the pulmonary route, an important drug administration route. Its NE formulation improved lung deposition and drug retention when used as an aerosol, preventing first-pass metabolism and improved therapeutic efficacy [70].

6.4 Oral delivery of LNE

Amphotericin B is capable of being distributed directly into the lungs owing to the pulmonary route, an important drug administration route. Its NE formulation improved lung deposition and drug retention when used as an aerosol, preventing first-pass metabolism and improved therapeutic efficacy [71]. Orally administered nano emulsion of PUFA derivatives bio-isosteres have demonstrated the potential to suppress growth and promote apoptosis in triple-negative human breast cancer cells MDA-MB-23 [72].

6.5 Topical delivery of LNE

Topical treatments experience challenges due to low the dispersibility or skin abrasive characteristics. Topical absorption has been explored applying NEs, which provide a concentration gradient and penetration enhancement [73]. For instance, a LNE comprising camphor, methyl salicylate, and menthol exhibited a high degree of penetration. A paclitaxel-containing NE demonstrated good availability with little systemic escape for deep skin application. Additionally, caffeine has been applied topically using a W/O NE to treat cancer of the skin [32, 74].

6.6 Vaccine delivery

In a strategy to deliver the vaccine, LNEs are essential. Their distinctive characteristics strengthen the immune response by facilitating the efficient encapsulation and distribution of antigens. In vaccine delivery LNE facilitates cellular absorption, improves stability and protection, and offers a diverse formulation choice [75].

7. Conclusion

LNEs are submicron lipid droplets that are employed for IV-injectable carriers for poorly soluble drugs and offers an array of platforms for administration of drugs and other medicinal purposes, owing to the ability they have to improve the solubility and bioavailability of therapeutic agents. Numerous manifestations of LNE provide several advantages adapted to particular therapeutic demands. There are a number of approaches are available to prepare the LNE discussed in this review. Since, it is economical to prepare LNE with therapeutic purposes, it could be explored for future therapeutics for which much more investigations still necessitate.

Abbreviations: LNE (Lipid nano-emulsion), API (Active pharmaceutical ingredient), DI (Deionized), DHA (Docosahexaenoic acid), DOTAP (1,2-dioleoyl-3-trimethylammonium propane), DOX (Doxorubicin), MCT (Medium chain triglyceride), NE (Nano emulsion), LDLP (Low density lipoprotein), FA (Folic acid), HEPC (Hydrogenated egg yolk phosphatidylcholine), IV (Intravenous), PFA (Polyunsaturated fatty acids), PTX (paclitaxel), PDI (Poly dispersity index), ZP (Zeta potential)

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