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A Review on Solid Lipid Nanocarriers for the Effective Treatment of Neoplasm

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Abstract:

Due to the numeral specific technical and substantial features, lipid based nanocarriers play an increasingly important role.Good examples of how to join the characteristics of the more known liposome structures, they are bio-consistency and biodecaying, with steadiness and composition versatility that are specific to nano carrier system made by polymers, are solid lipid nanoparticles, lipid nanocapsules and nanostructured lipid carriers, and drug – lipid conjugates.In addition, combining chemical treatments with nanoparticles with lipid substances decreasesthe beneficial dose and toxicity, reduces resistance to drugs and enhance tumor tissue medicine levels by decreasing them at healthy tissue. Lipid based nano particles are thoroughly tested in in-vitro but also in vivo in some clinical tests with promising results. This review summarizes the LBNP types developed in recent years and the main findings for treatment with cancer, including critical tests in patients.

Key words*: Solid lipid nano particles, Liposomes, lipid based nano carriers.*

1. Introduction:

In developed and developing countries neoplasm is the first headed cause of death, responsible for 7.6 million deaths (roughly13% of all deaths)[1].It is the main reasonfor deaths all over universe even though there is availability of several treatment options like surgery, treatment with some chemo preventive chemical substance, therapy by UVrays (radiation) which causes inflammation to the nearer tissues or organs, apart from these there is also availability of immune therapy[2]. Treatment with chemotherapy mainly contains chemical substances that hamper with cell division and protein synthesis which results in cell fatality[3].There are various disadvantages with the prolonged usage of present therapeutic agents which are used for the treatment of neoplasm such as normal cell toxicity, undesirable action, unexpected increase in drug intensification at the target tissue, and also increase in the resistance of the agent with continuous use of these anticarcinogens[4].The treatment of cancer by this traditional route will affect the normal cells along with the cancer cells which leads to various unwanted effects like vomiting, nausea, dizziness, nephrotoxicity, diarrhea, fatigue, alopecia, insomnia, weight loss,

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loss of apatite and cardio toxicity[5]. There is an immediate need for new delivery systems for the advancement of the present treatment options and to reduce the adverse effects. The aim of nanotechnology for cancer is to discover new technologies which can improve the advance treatment options or to enhancepresently using therapeutic options by reducing the toxicities[6]. Variousneoplasmic drugs have limited use because of their toxicity, poor solubility, nonspecificity, rapid elimination, and other unusual adverse reactions[7], Even thoughpresently, there are manyimprovements are made in the area of drug releasein sort to overcome the boundaries caused by the neoplasmic agents[8].The usefulness of traditional chemotherapy is restricted by the following restrictions, even when new molecules are discovered to treat cancer: i) Tumor-level drug resistance due to obstacles (i.e. non-cell-based mechanisms). ii) Cellular drug resistance (i.e. cell mechanism). iii) Biotransformation and quick clearance in the body for non-specific distribution of anticancer drugs[1].

2. LIPID BASED FORMULATIONS AND NANOPARTICLES:

The newly introduced Neoplastic agents which have poor water solublility and poor oral bioavailability belongs to BCS class II [9].Lipids as carrier systems have gained great interest in the delivery of various anti carcinogens with poor solubility and bioavailability.The lipid based nanocarriers will protect the neoplastic agents from the degradation from various enzymes, and also help in sustained and controlled release of neoplastic agents, that results in the production of nano carriers from the lipid[10]. The neoplastic agents are taken care by the lipid based nanocarriers from the degradation by various enzymes, and also help in improvement of lipid-based nano formulations.In the late 1970s, the origin of the ‘nano era ‘led to the development of many different devices in the nanometer scale and is known as nano drug delivery system.Nanoemulsions, suspensions, lipid nanocapsule (LNC), hybrid particles oflipid-polymers, niosomes, spherules, solid-lipid nanospheres, nanostructured lipid carriers (NLCs), etc are the examples of lipid-based formulations which play a vital role in neoplasm treatment[1].

Nanoscale level research vows to offer new plans to address the absolute most perplexing human maladies at the sub-atomic level for huge upgrades in infection aversion, finding and treatment[11]. For simultaneous drug delivery and molecular imaging, lipid formulations need to use nanometer-scale particles for some best applications.There are one of a kind chances to utilize lipid-based nanoparticles (LNPs) for both symptomatic and helpful purposes[12].

3. LIPID BASED NANO CARRIERS FOR NEOPLASM TREATMENT:

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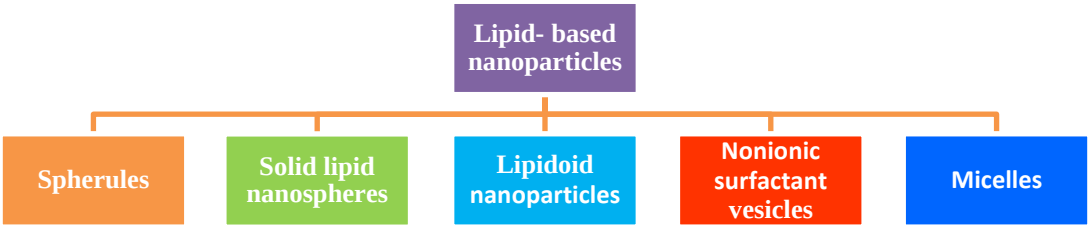

Fig 1:Lipid based nanocarriers

3.1.SPHERULES:

Spherules, at first known as liposomes, are among the most progressive medication conveyance frameworks.They are a controlled self-get together of amphipathic lipids that structure circular lipid bilayer, encasing a fluid inside moiety for the tranquilizing epitome[13]Liposomes are considered as original particles of lipid-based nanoparticles and are one of the main medication conveyance frameworks presented [14]. Gregoriadis was the first person to use liposomes as drug delivery systems to deliver antineoplasmic and anti microbial drugs to tissues[15, 16].

3.1.1. Components of Liposome's:

The main components of liposomes are phospholipids and cholesterolPhospholipids are the fundamental atomic structure squares of the liposome. Phospholipids are the fundamental atomic structure squares of the liposome. The phospholipid is a lipid that is Amphiphatic which comprise of the hydrophilic polar head and hydrophobic tails thus have a proclivity for both watery and polar moiety for example both hydrophilic medications can be epitomized in the watery stage and hydrophobic medication atoms can be consolidated in the lipid bilayers.Most commonly used phodpholipids are phophotidylcholine and phophatidylethanolamine. Therefore liposomes can encapsulate both water soluble and water insoluble anticancer agents[17].

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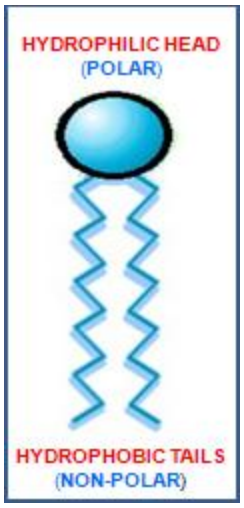
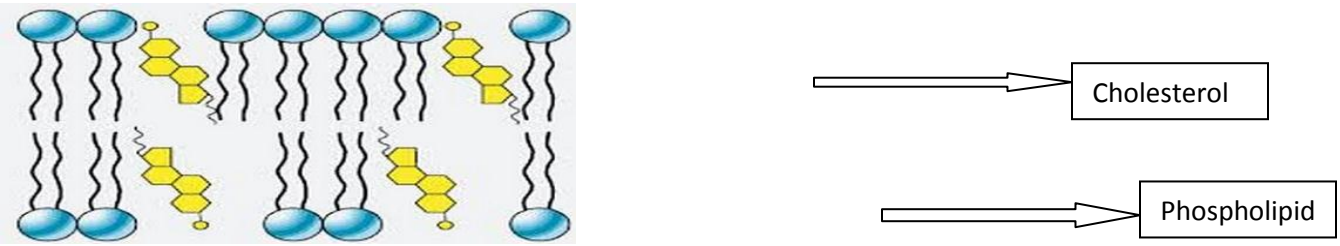


Phospholipid

The second component cholesterol is a steroid lipid which mainly stabilizes the membrane and interdigitates between the phospholipids. The cholesterol makes the membrane less ordered below the transition temperature and more ordered above the transition temperature[18].



Interdigitation of cholesterol between the phospholipids

Role of cholesterol in the lipid layer formation:[19].

- ✓ Cholesterol acts as a fluidity buffer
- ✓ After intercalation with the phospholipids molecules it alters freedom of motion of the carbon molecules in the acyl chain.
- ✓ Cholesterol mainly increases the stability of the bilayer membrane.
- ✓ Cholesterol is incorporated in to the phospholipid layer in the ratio of 1:1 or 2:1 (cholesterol- phospholipids)
- ✓ It restricts the transformation of trans to gauche conformations.

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- ✓ It upgrades the unbending nature of the phospholipid bilayer
- ✓ It likewise decreases the porousness of the water solvent substances.

3.1.2. STRUCTURE OF LIPOSOME:

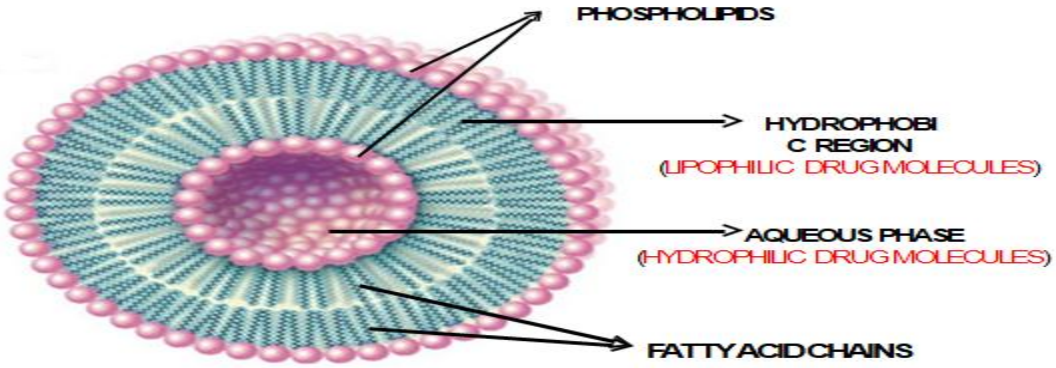

Fig 2: Structure of liposome

3.1.3. FORMULATION MECHANISM OF LIPOSOMES[20]:

Phospholipids are insoluble in aqueous media so they systematizethemselves closely in planar bilayer sheets or lipid cakes which areheat stable.In which hydrophobic chains turns inner side to avoid the water phase and polar head bunches face outwards into the watery medium, offering ascend to twofold layer. This double layerconstruction is also known as lamella.

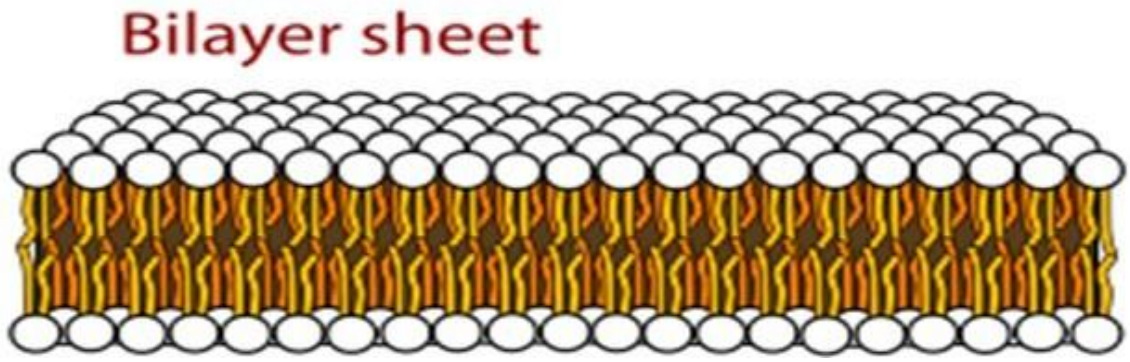

Fig 3: Structure of bilayer

Upon further hydration, the lipid cakes (lamella) expands, in the long run, they bend to shape shut vesicles as circles. These circles are called liposomes.

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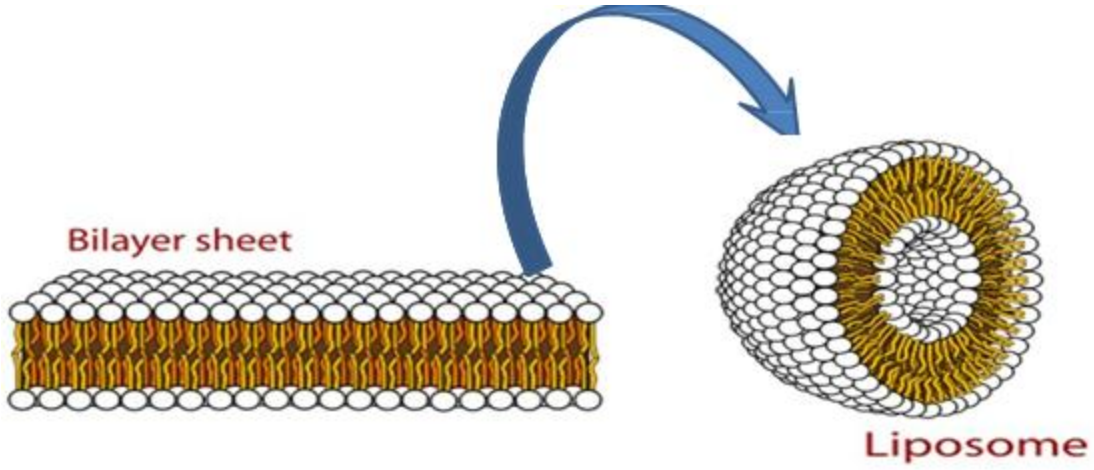

Fig 4: Formation of liposome

3.1.4. TYPES OF LIPOSOMES[21]:

In light of their molecule size and the quantity of the lipid bilayers, liposomes are ordered into:

1. The Single lipid bilayer particles with size frequency of 20-100nm is known as Unilamellar Vesicles (SUVs).
2. Single lipid bilayer particles with frequency of 100 nm is known as Large unilamellar vesicles (LUVs).
3. Giant unilamellate vesicles (GUVs) are particle sized vesicles of 1000 nm.
4. Multilayered vesicles (MLVs) are several unilamellated vesicles framed inside one another and isolated by fluid stage, and have particle size 0.5–10 μm.

Liposome can be classified into three forms on the basis of surface charge:

1. Positively charged liposome's
2. Negatively charged liposome's
3. Neither positively nor negatively charged liposome's

Positively charged liposomes

Positively charged liposomes are produced with lipids which give the liposome surface a positive charge. Stable compounds with negative therapeutic agents like iRNA can form lipolexes [22-23]. These cationic liposomes have common characteristics of water solubility and high pH loading density physiology. Therefore, cationic liposome can interact with loaded target cell surfaces that can increase cell contact and absorption[24].

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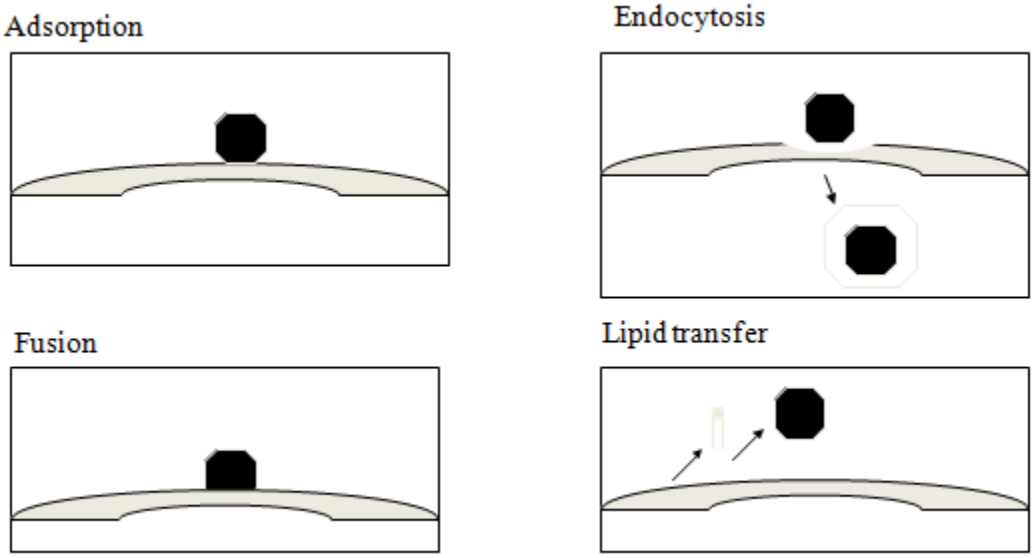
Negatively charged liposomes:

The anionic liposomes are prepared from the anionic head phospholipids, which are the principle parts of cell layers and are required for intracellular piraty and film steadiness[25]. Of course, negative charged lipid occurs in cell mucosa and plays acrucial role in cell signs, lipid-protein association and layer dealing, including phosphatidyl glycerol, phosphatidyl ionositol, phosphatidic acid and PS [26].

Neutral liposomes:

Neutral liposomes from neutral lipids are prepared. Large lipids for negative charges such as siRNA have first been used for the supply of drugs. In addition to the demand for success in genetic material formulation, the main challenge remains the toxicity of the negatively charged component and lipid.The toxicity and further harmsrelatedamong CTL amongelevatedrelease efficiency for products like SiRNA have been found to overcome Neutral liposome, composed by neutral lipids[27-28]. Low-toxicity, increased blood circulation, less communication with proteins, no RES absorption and no provocative cytokine inductions are high safety profiles of neutral liposomes [29-30]. The wellbeingsummary is extremelybeautiful to neutral liposomes for systemic release.

Modes of liposome and cell interaction:



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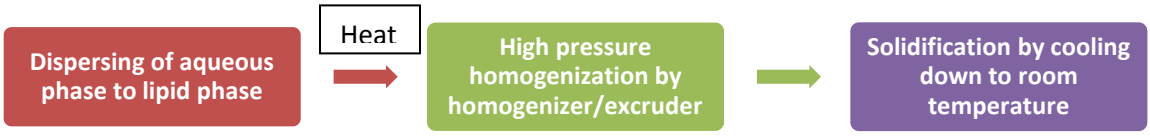
4. SOLID LIPID NANOPARTICLES:

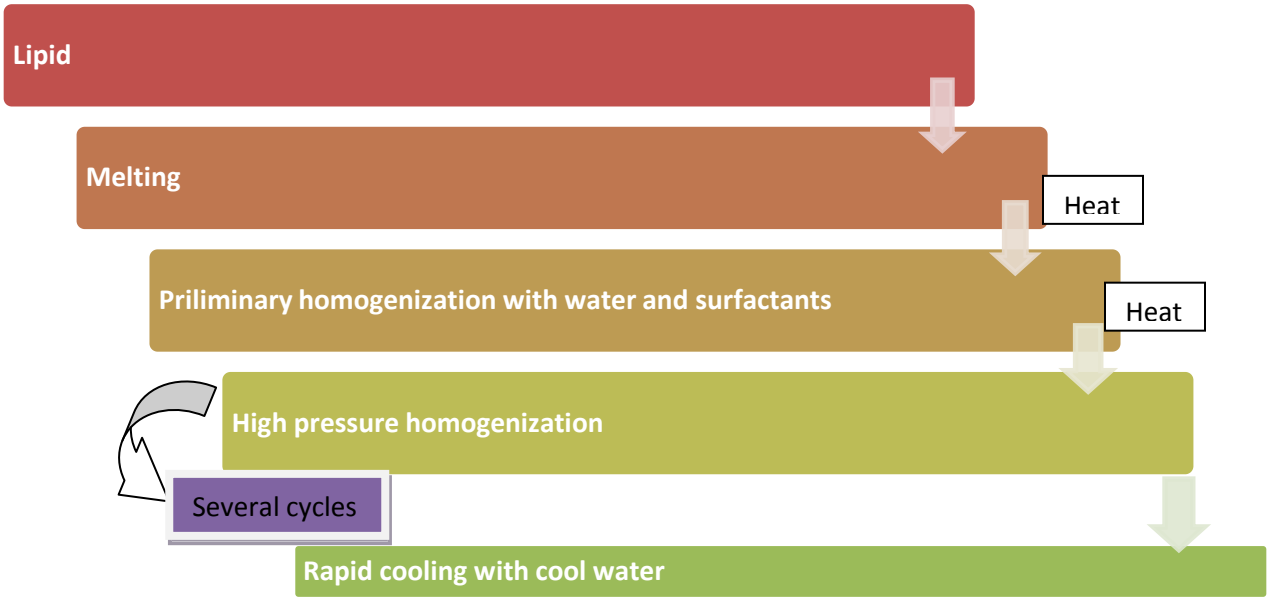
Solid lipid nanoparticle (SLN) is an substitute to conventional colloidal carrier systems and consists of physiologically tolerated solid lipid dispersed into water soluble surfactant solution within a frequency of of 100 –150 nm.[31]. The synthesis of solid lipid nano particles consists of lipids which are solid such as mono and di or triglycerides, phospholipids, lipid, Glyceride mixtures or waxes and cholesterol [32]. Lipid-medicate conjugate nanoparticles and nanostructured lipid transporters are able to deliver hydrophilic and ionic compounds.SLNs are able to protect labile anticancer drugs.SLNs have major benefits, including site-specific targeting, long-term physical stability, the opportunity of controlled releases of water soluble and water insoluble medicines, labile drug guard, low cost, ease of preparation as well as no toxicity [33].

4.1.PREPARATION OF SOLID LIPID NANO PARTICLES[34-35]:

Hot homogenization:



High pressure homogenization:



Solvent evaporation:

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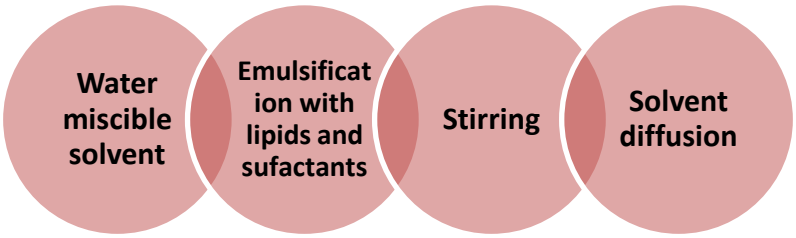
Solvent emulsification-diffusion:



Microencapsulation:

Fig 6: Preparation methods of solid lipid nano particles

5. LIPIDOID NANOPARTICLE

These are the conventional class of lipid-based nanoparticles that utilization cholesterol and PEG-covered lipids. Lipidoid particles are blended from straight acrylic alkane esters or epoxy subordinates with amine mixes by means of added substance responses set up a compound strategy to permit quick combination of an expansive lipidoid library that can be utilized for the conveyance of siRNA [36].

6. NONIONIC SURFACTANT VESICLES (NSV)

As far as structure, NSV, otherwise called niosomes, are lipid-based particles like liposomes, as they comprise of a fluid moiety typified by lipid bilayers that empowers them to epitomize medications and fill in as medication transporters [37]. The cosmetics industry first created niosomes and since then, as a drug delivery system, have increased interest. NSV are self-assembly vesicles made ofpolyglycerol ether and cholesterol nonionic surfactants, next tothe other components like charging agents [38]. Esters of sorbitan fatty acids, polyoxyethylene fatty

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acid esters, alkyl ethers, and alkyl glyceryl ethers [39] are widely used to prepare niosomes. Such surfactants are both hydrophilic head and hydrophobic tails amphiphilic molecules. In their hydrophilic heads, these compounds have no charged groups. Like liposomes, the two layer structure of niosomes allowwater soluble substances to be encapsulated in their aqueous core and hydrophobic molecules in their lipid bilayer[40].

7. MICELLES:[39]

Micelles are suddenly framed by amphipathic atoms, colloidal structures. The type of these amphiphilic atoms decides if lipid micelles, polymeric micelles or lipid-polymeric half breed micelles are the subsequent class of micelles. While liposomes or niosomes have a lipid bilayer structure which embodies a fluid moiety, lipid micelles shape a monolayer with lipophilic tails which structure the inward center and hydrophilic heads that are presented to the watery setting.Contingent upon their organization, micelles may differ fit as a fiddle from circular pole like or ellipsoidal structures [41]. Basic micelle focus (CMC) is the most minimal grouping of amphiphilic particles at which micelles are framed; at this fixation these atoms start to shape the micellar structure, a get together determined by the lessening of free vitality. Micelles are normally utilized as nanocarriers for hydrophobic medication conveyance, which is situated in the micellar structure's inward center [42].

8. NANO STRUCTURED LIPID CARRIERS (NLC):

NLCs correspond to a nextage group of lipid-based SLN-based nanocarriers, consisting of a blend of solid and fluid lipids. In order to overcome the limitations of SLNs, this system was developed to provide increased drug load capacity to NLCs and to prevent drug expulsion during storage by preventing lipid crystallisation due to the presence of liquid lipids in the formulation of NLC during storage[43].

Nanostructured lipid carriers (NLCs) consisting of a lipid matrix with a common nanostructure. This nanostructure enhances drug loading and during storage firmly incorporates the drug. These NLCs can be produced by homogenizing high pressure and the process can be modified to produce 30–80 percent lipid particle dispersion with solid content.Different types of NLCs are obtained depending on the manufacturing method and the lipid blend composition. The basic idea is to enhance the consignment for active compound by giving a certain nanostructure to the lipid matrix and avoid expulsion of the compound during storage.

Methods of preparation of NLC:

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1. By the method of high pressure homogenization
2. By the method of solvent-Emulsification method
3. By Microemuslsification technique
4. By ultrasonication
5. By phase inversion
6. By solvent-emulsification diffusion
7. By multiple emulsion techniques.
8. By membrane contractor technique[44].

Lipid screening for the preparation of NLC:

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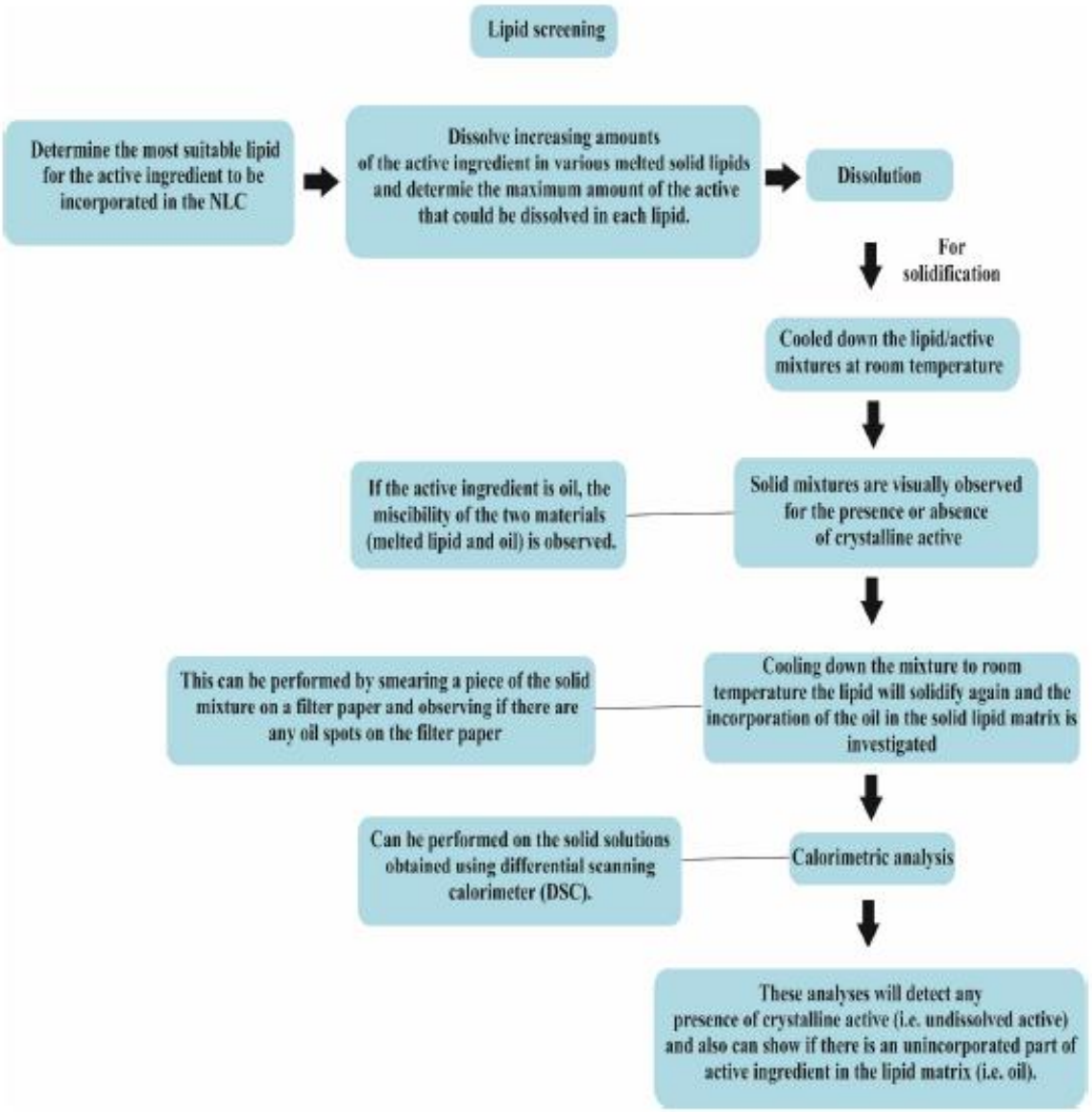

High pressure homogenization:

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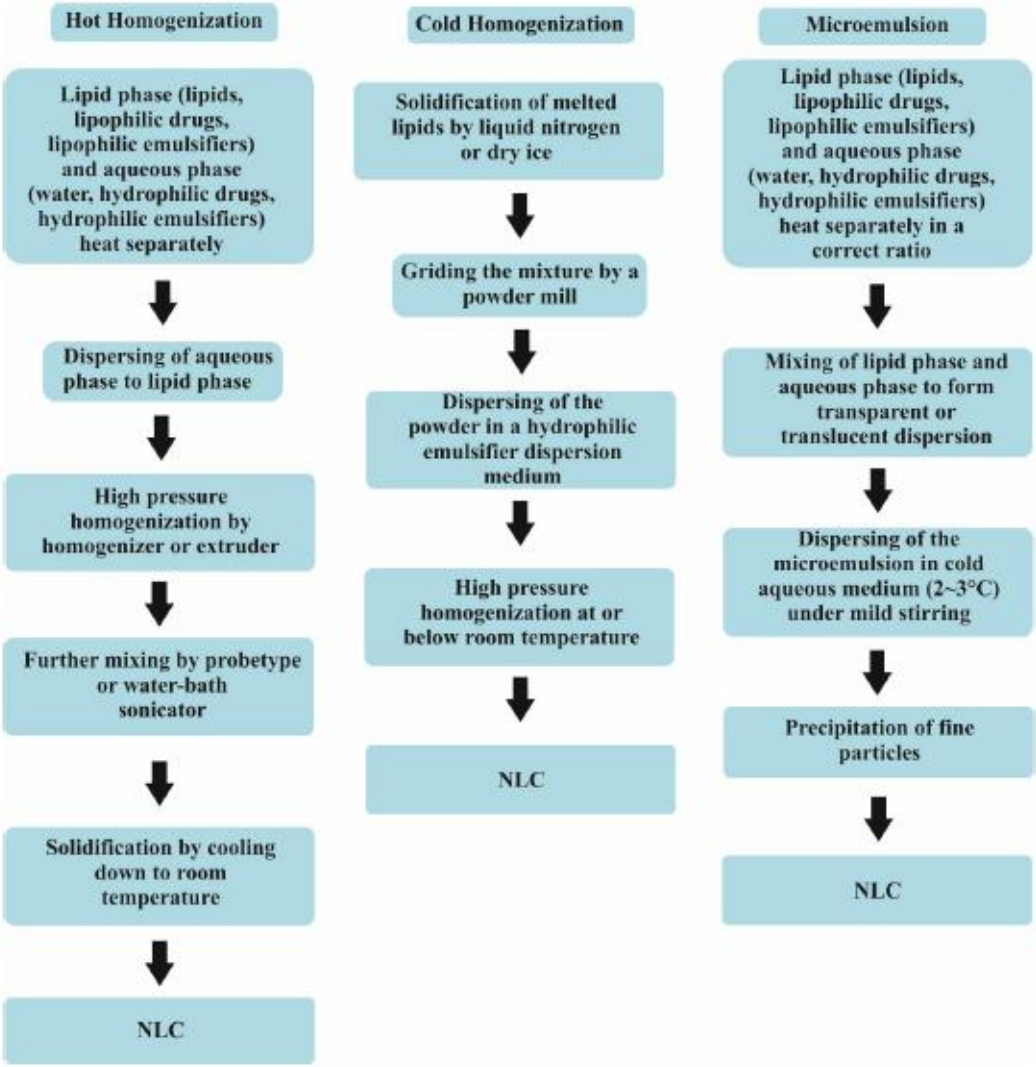

9. Advantages Of Lipid Based Nanocarriers[45]:

- They have both targeted drug release and controlled drug release.
- They enhance the stability of various pharmaceuticals.
- Compared to other carriers theyhave high enhanced drug content.
- Both water-soluble and water-insoluble drugs can be carried.
- As most lipids are biodegradable solid lipid nano particles are excellent carrier systems.
- All the solid lipid nano carriers are biocompatible.
- They will not use any organic solvents because they used water based technology.
- Less expensive than surfactant based carriers.
- Lipid based nano carriers are easy to validate and approval.

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