Available online at www.jcsonline.in
Journal of Current Science & Humanities 9 (2), 2021, 1-11.

Impact Factor- 2.05

SOLIDLIPIDNANOPARTICLES:APROMISING DRUG DELIVERY SYSTEM

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ABSTRACTAs an alternative to other typical colloidal carriers such as liposomes, polymeric nanoparticles, and emulsions, solid lipid nanoparticles are at the forefront of the rapidly expanding area of nanotechnology.With greater stability, they provide benefits such as controlled medication release and tailored drug delivery.Purpose: Dispersed in water or an aqueous surfactant solution, solid lipid nanoparticles (SLNs) are composed of spherical solid lipid particles in the nanometer size range. The use of SLN technology to transport hydrophilic and lipophilic medicines is an exciting new development.Nanoparticles present an opportunity to develop new therapeutics because of their unique size and reliance on lipids.Incorporating medicines into non-carriers provides a novel model for drug delivery that might be used to several levels of drug targeting.Researchers have shown a lot of interest in solid lipid nanoparticles because of the potential they offer to achieve the objective of regulated and site-specific medication delivery. Summary: This review paper covers the possible benefits and drawbacks, excipients, and various techniques used in their manufacturing, characterization, and uses. New possibilities in the treatment of complicated illnesses may emerge from SLNs if they are well studied. Models of drug integration into SLN and SLN release pattern get special consideration.

Keywords: Solidlipidnanoparticle, Targeteddrugdelivery,Production, Characterization,*etc.*

INTRODUCTION:

The field of Novel Drug Delivery System is emerging at an exponential rate with the deep understanding gained in diversified fields of Biotechnology, Biomedical Engineering and Nanotechnology [1]. Nanotechnology is a newer development technology expected to bring revolutionary changes in the field of life sciences. Nanotechnology, as defined by the National Nanotechnology Initiative (NNI), is the study and use of structures roughlyin the size range of 1 - 100 nm.

Nanotechnology is the science of matter and material that deal with the particle size in nanometers. These are small scale colloidal particles that are made of non biodegradable and biodegradablepolymersandtheirdiameterisabout 200 nm. The important goals for research of nanotechnologies in drug delivery include:

a. Reduction in toxicity while maintaining therapeutic effects,
b. Specificdrugtargetingand delivery,
c. Biocompatibleandmoresafety,and
d. Developmentofsafe medicines.

Nanoparticles are solid polymeric, submicronic colloidal system range between 5 - 300 nm consistingof macromolecular substances that differ in size 10 nm - 1000 nm. The drug of interest is dissolved,entrappedadsorbed,attachedor encapsulated into the nanoparticle matrix [2]. They are manufactured from synthetic / natural polymers and ideally suited to optimize drug delivery and reduce toxicity.

The advantages of using nano particles for nanoparticles loaded with drugs, because of their

small scale size can penetrate through small capillaries and are taken up by cells and allow the drug release at appropriate rate and dose at specific sites in the body for a certain time to release the accurate delivery, which enhances the therapeutic response and reduces the toxicity and side effects. Theuseofbiodegradable material fornanoparticles preparation allows sustained release at the target site over a period of days or even weeks. In the middle of the 1990s, different research Groupshave focused on different nanoparticles made from solidlipids,calledassolidlipidnanoparticles(SLN or lipospheres or nanospheres) Solid lipoid nanoparticles are one of the novel potential colloidal carriers [3] systems in the range of 100 - 150 nm as alternative materials to polymers which is identical to oil in water emulsion for parenteral nutrition, but the liquid lipid of the emulsion has been replaced by a solid lipid [4].

Advantages: SLNs combine the advantages and avoid the disadvantages of other colloidal carriers.

a. SLNsparticularlyrangingbetween120nm and 200 nm are not taken up readily by the cells present in the RES (Reticulo Endothelial System), thereby bypassing liver and spleen filtration [4].
b. It is possible for controlled drug release andsite specific drug targeting. Increased scope of drug targeting can be achieved by coating with or attaching ligands to SLNs
c. It is suitable for lipophillic as well as hydrophilic compounds [5].
d. Organicsolventsareavoided [6].
e. It is less toxic than some polymeric nanoparticles because used lipids are physiological and biocompatible [2,7].
f. Itisflexibleinsterilization[8].
g. Low cost for solid lipid as compared to biodegradable polymers and phospholipids.
h. Ease of manufacture and scale up. It is easy to manufacture than bipolymeric nanoparticles.
i. Better control over release kinetics of encapsulated compound.
j. TheSLNshave enhancedstabilityas compared to the other colloidal carrier systems.
k. Solid lipid nanoparticle as colloidal drug delivery is suitable for different routes of administration like oral, pulmonary, rectal, ophthalmic, dermal and parenterals administra- tion, *etc*.
l. Protection of drugs sensitive and liable for photochemical, chemical or oxidative degrada- tion.
m. Excellent reproducibility with use of different methods as the preparation procedure [9].
n. SLNs can enhance the bioavailability of entrapped bioactive materials.

Disadvantagesof SLN:

a. SLNshavepoor drugloadingcapacity[10].
b. Polymeric transitions during storage may lead to the drug expulsion from the nanoparticles.
c. The low capacity to load water soluble drugs due to partitioning effects during theproduction process.
d. They have relatively higher water content. (70- 99.9%) [11].

General Ingredients: It includes solid lipid(s), Emulsifier(s), and water. The lipid is used here like triglycerides,partial glycerides,fattyacids,steroids etc. The emulsifiers have been used to stabilize the lipid dispersion. The choice of emulsifier depends on the administration of drug, to the parenteral system;there arelimitstochoosetheemulsifiers[12].

Production Method of Solid LipidNanoparticles:

1. High Pressure Homogenization (HPH): In this method lipids are pushed with 100 - 200 bars high pressure through a narrow gap of few microns ranges. Disruption of particles to submicron ranges occur because of the shear stress and cavitations force (due to sudden changes in pressure). Lipid content in the range 5 - 10% normally. This technique is used for nanoemulsion and PTN.There are 2 basic production methods by high pressure homogenization: Hot homogenization and cold Homogenization. In these both techniques, drug is dispersed or solubilized in the lipids above their melting points [13].

A. Hot Homogenization: Lipid components are the first melted by heating above melting point. Therefore it can be regarded as homogenization of an emulsion. Drug is either dispersed or dissolved in molten lipids. Then aqueous surfactant is added at the same temperature. This pre-emulsion of the drug loaded lipid melt and aqueous surfactantphaseis obtained with high shearingdevice such as ultra turrax. High pressure homogenization of pre-emulsionistakenatthetemperaturehigherthanthe melting point of lipid. While increasingtemperature heat accelerated drug degradation occurs.Theprocessiscontinuedtilldesiredparticle size. 3 - 5 homogenization cycle are sufficient for requisite particle size. After homogenization the nanoemulsion is formed due to liquid nature of lipid. This on cooling gives rise to solid lipid Nanoparticles. This technique is advantage for suitable for scale up [13].

B. Cold homogenization: This method has been developed to overcome the problems that occur in hot homogenization.

a. Drugdistributionintoaqueousphaseduring homogenization.
b. Temperatureinduceddrugdegradation.

Step1:PreparationofMicro-emulsion:

c. Complexity of crystallization step of nanoe / or super cooled melts [14,15].

Hot and cold method steps and shown in **Table 1**. In comparison to hot homogenization in cold homogenization particle size and polydispersity index are more.

2. Micro-emulsion Technique: Gasco and co-workers were the first to develop solid lipid nanoparticles based on the dilution of micro-emulsions. Micro emulsions are clear, thermo-dynamicallystable, isotropic system composed of a lipophilic phase, surfactant and co-surfactant (in most cases) and water. The concept of microemulsion technique for the production ofSLN was developed and optimized by Lipids used to prepareSLNsaresolidsat roomtemperatureand hence the microemulsion is prepared at a temperature above the melting point of the lipid. Both thelipid andtheaqueousphasecontainingthe emulsifier are mixed in appropriate ratios and stirredsothatit will producea microemulsion. **Fig. 1** and **2** Shows the Micro-emulsion process steps used for SLN production.

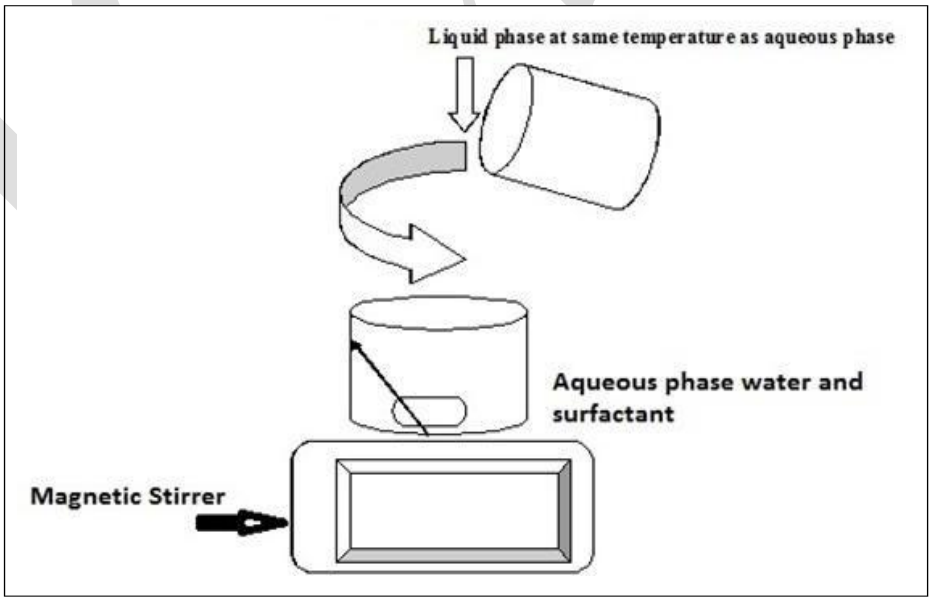


FIG.1:STEP1MICRO-EMULSION

Step2:Formationof Solid Lipid Nanoparticle:

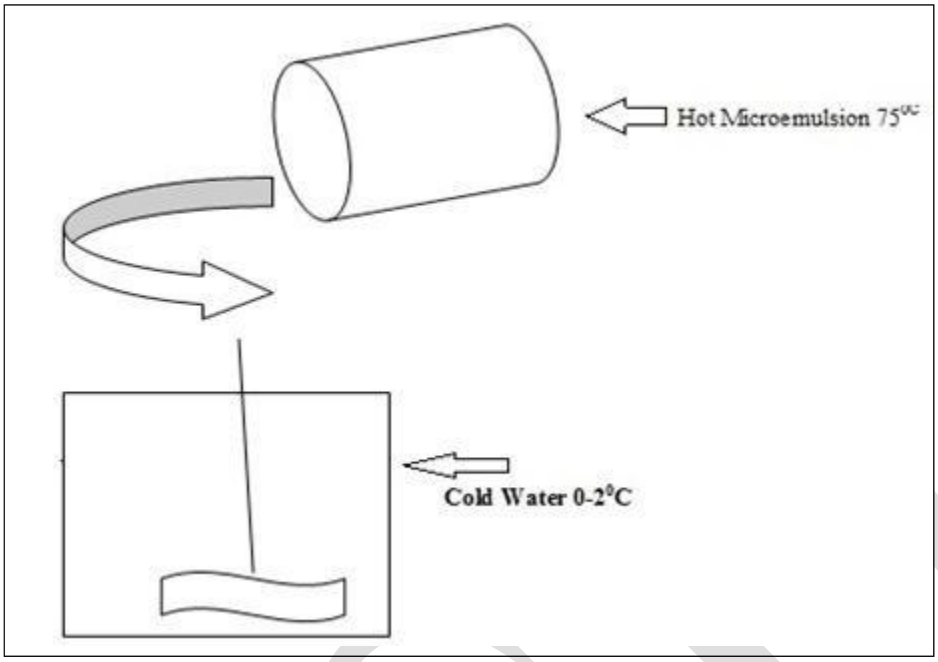


FIG.2:STEP2OFMICRO-EMULSION TABLE

1: STEPS OF COLD AND HOT HOMOGENIZATION TECHNIQUE

	ColdHomogenization	HotHomogenization
Step1	Meltingoflipid5-10ºCabovethemelting point	
Step2	Dissolve/Dispersedruginmeltedlipid.	
Step3	Rapidlycooledtosolidifythedrugloaded lipidinliquidnitrogenordryice.	Dispersingdrugloadedlipidinaqueoussurfactant solution
Step4	Solidlipiddrugmilledtomicronsize(50-100 µ)	Highspeedstirrerusedtopremixandpreemulsion formed
Step5	Dispersedthemilledpowderinaqueous surfactantsolutiontoformapre mix.	Highpressurehomogenizationatatemperatureabove lipidmeltingpoint
Step6	HighPressurehomogenizationinroom temperatureorbelowroomtemperature SolidLipidNanoparticles	Hoto/wnanoemulsion.Recrystallizationof nanoemulsionbycoolingtoroomtemperature

3. Solvent Emulsification - Diffusion Technique: Another technique which is proposed forproduction of solid lipid nanoparticles is solvent emulsification-diffusion method [16,17]. In this technique,thesolvent usedlike *e.g.* benzyl alcohol, butyl lactate, ethyl acetate, isopropyl acetate, methyl acetate must be partially miscible with water. This technique can be carried out either in aqueous phase or in oil phase [13,18]. Initially, both the solvent and water were mutually saturated in order to establish the initial thermodynamic equilibrium of both liquid [38]. When heating is required to solubilize the lipid, saturation step was performed at that temperature. Then the lipid and drug were dissolved in water saturated solvent and this organic phase which is internal phase was emulsified with solvent saturated aqueous solution containingstabilizer*i.e.*dispersedphaseusing mechanical stirrer. After the formation of o/w emulsion, water is a dilution medium in typicalratio ranges from 1:5 to 1:10, added to the systemin order to allow solvent diffusion into the continuous phase, and forming aggregation of the lipid in the nanoparticles. Avoidance of heat during the preparation is the most important advantage of this technique.

4. Solvent Emulsification or Evaporation: In this method, the production of nanoparticle dispersions by precipitation in o/w emulsions. The lipophilic material and hydrophobic drug is dissolved in water-immiscible organic solvents like *e.g.* cyclohexane,dichloromethane,toluene,chloroform *etc* and then that is emulsified in an aqueous phase using high speed homogenizer [19,20]. Upon evaporationofthesolvent,nanoparticledispersion is formed by lipid precipitation in the aqueous medium. Thereafter, the organic solvent was evaporated by mechanical stirring at room temperature and decreased pressure (*e.g.* rotary evaporator) leaving lipid precipitates. Here, the mean particle size depends on the lipid concentration in organic phase. Very small particle size could be obtained with low lipid content (5%) related to organic solvent.

5. Ultrasonication: Ultrasonication or high speed homogenization is one of the methods for the production of SLNs. The advantage of this method is that the equipment used is easily available at lab scale. However, this method suffers from problems such as extensive size distribution ranging into micrometer range. Potential metal contaminations, physical instability like particle growth upon storage are other drawbacks associated with this technique.

6. Supercritical Fluid (SCF) Technology: More recently, attractive new techniques based on SCF technology have been studied as useful alternatives fordryingpharmaceuticalproteinformulations,and to produce solvent-free particulate drug carriers [5]. The main advantages of such techniques include possible sterilizing properties of supercritical CO_2 and mild processing conditions, ability ofproducing microparticles or nanoparticles in the form of dry powders and feasibility of scaling-up**.** Carbon dioxide (CO_2) has been used almost exclusively in SCF processing of pharmaceuticals because of its low toxicity, moderate critical pressure and its relatively low critical temperature, and its low cost.

7. Solvent Injection Technique: In this technique, the solid lipid is dissolved in water miscible solvent. The lipid solvent mixture is injected into stirred aqueous phase with or without surfactant. Finally, the dispersion is filtered to remove excess lipid. Emulsion within the aqueous phase aids to producelipiddropletsatthesiteofinjectionand stabilize SLNs until solvent diffusion completes [21,22].

8. Spray Drying: It is an alternative tool to lyophilization in order to transform an aqueousSLN dispersion into a drug product. This is an economicmethodthanlyophilizationand

recommendstheuseoflipidwithmeltingpoint >70°C. This method causes particle agglomeration due to high temperature,shear forces and partial melting of the particle.

9. Melting Dispersion Technique: In this technique drug and solid lipid were melted in an organic solvent which is termed as oil phase and simultaneously water phase was also heated tosametemperatureasoilphase.Thentheoilphasei s added slowly in to a small volume of water phase with stirringat higher rpm for few hrs. Then, it was cooled down to room temperature to produceSLNs. Reproducibility was more than ultrasonication method but lesser than that of solvent emulsification evaporation method [23].

10. Double Emulsion Technique: In double emulsion technique the drug was dissolved in aqueous solution, and then was emulsified in molten lipid. This primary emulsion was stabilized by adding stabilizer (*e.g.* poloxamer - 407). Then stabilized primary emulsion was dispersed in aqueous phase containing hydrophilic emulsifier. Then, the double emulsion was stirred and was isolated by filtration.

11. Membrane Contactor Technique: In this technique, the liquid phase was pressed at a temperature above the melting point of the lipid through the membrane pores allowing theformationofsmalldroplets.Theadvantagesoft his, the control of the SLN particle size by proper choice of process parameters. The aqueous phase was stirred continuouslyandcirculatedtangentially into the membrane module, and sweeps away the droplets being formed at the pore outlets. SLNs were formed by cooling of the preparation at the room temperature. Here both the aqueous and organic phases were placed in the thermostatedbath to maintain the required temperature and nitrogen was used to create the pressure for the liquid phase. Vitamin E loaded SLN was prepared using this technique to allow large scale production and their stability is demonstrated.

12. Precipitation Technique: Solid lipid nanoparticles can also be produced by a precipitation method which is characterized by the need for solvents. The glycerides will be dissolved inanorganicsolventlikechloroformandthe solution will be emulsified in an aqueous phase. After evaporation of the organic solvent, the lipid will be precipitated forming nanoparticles.

Characterization of SLN: Characterization of the SLNs is necessary for its quality control. However, characterization of SLN is a challenge due to the colloidal size of the particles and the complexity and dynamic nature of the delivery system.

1. Measurement of Particle Size and Zeta Potential: The physical stability of SLNs depends on their size. Photon correlation spectroscopy(PCS) and laser diffraction (LD) are the most effective techniques for determination of particle size. PCS also known as dynamic light scattering measures the variation in the intensity of the scattered light, which is occurred by particle movement. The particle size determination by photon correlation spectroscopy (PCS) detects size range of 3 nm to 3 μm and by laser diffraction in sizerangeof100nmto 180μm.AlthoughPCSisa good device to characterize nano-particles it is capable forthedetection oflargermicroparticles [24].

Zeta potential analyzer or zetameter is used to measure the zeta potential. Before measurement, SLN dispersions are diluted 50 times with the original dispersion preparation medium for size determination and zeta potential measurement [25]. A high value of zeta potential may lead to deaggregation of particles in the absence of other complicating factors such as hydrophilic surface appendages or steric stabilizers. Zeta potential measurements can be useful for predictions about the storage stability of colloidal dispersions.

A. Electron Microscopy: Transmission electron microscopy (TEM) and Scanning electron microscopy (SEM) provide way to directly observe nanoparticles. However, SEM is better for morphological examination. TEM has a small size limit of detection [26].

B. Dynamic Light Scattering (DLS): DLS also known as PCS records the variation in the intensity of the scattered light on the microsecond

timescale.

C. Static Light Scattering (SLS) / Fraunhofer Diffraction:SLSisanensemblemethodinwhich the light scattered from a solution of particles is collected and fit into fundamental primaryvariable.

D. Acoustic Methods: It measures the attenuation of the scattered sound waves as a means of determining size through the fitting of physically relevant equations.

E. Nuclear Magnetic Resonance (NMR): NMR can be used to determine both the size and qualitative nature of nanoparticles.

F. Atomic Force Microscopy (AFM): A probe tip with atomic scale sharpness is rastered across a sample to produce a topological map based on forces at play between the tip and the surface [14,27].

2. Measurement of Crystallinity and Lipid Modifications:

X-ray Diffraction (Powder X-ray Diffraction) and Differential Scanning Calorimetry (DSC): The geometric scattering of radiation from crystal planes within a solid allow the presence or absence of the former to be determined thus permitting the degree of crystallinity to be assessed. DSC can be used to determine the nature and the speciation of crystallinity within nanoparticles through the measurement of glass and melting point temperature. Thermodynamic stability, lipid packing density and quantification are a serious challenge due to the increase, while drug incorporation rates decrease in the following order:

Super cooled melt < α-modification < β9-modification < β-modification.

3. Co - existence of Additional Structures: The magnetic resonance techniques, nuclear magnetic resonance (NMR) and electron spin resonance (ESR) are powerful tools to investigate dynamic phenomena and the nano-compartments in the colloidal lipid dispersions. Dilution of the original SLN dispersion with water might cause theremoval of the surfactant molecules from the particle surface and induce further changes such as crystallization changes of the lipid modification [28].

4. Entrapment Efficiency: The entrapment efficiency of the drug is determined by measuring the concentration of free drug in the dispersion medium. Ultracentrifugation was carried out usingCentrisart, which consist of filter membrane (molecular weight cutoff 20,000 Da) at the base of the sample recovery chamber. The SLNs alongwith encapsulated drug remain in the outerchamber and aqueous phase moves into the sample recovery chamber. The amount of the drug present in the aqueous phase is determined by HPLC orUV spectrophotometer.

% Entrapment efficiency = [(Initial drug weight– weight of free drug) / Weight of initial drug] × 100%

5. *In-vitro* drug release: *In-vitro* drug release studies are used for quality control studies as well as for the prediction of *in-vivo* kinetics. In this SLN's due to very small size of the particles, the releaserateobserved*in-vivo*candiffergreatlyfrom the release obtained in buffer solution. Hence in-vitro release studies remain useful for quality control as well as for evaluation of influence of process parameters on release rate of active components.

a. Dialysis Tubing: *In vitro* drug release could be achieved using dialysis tubing. The SLNs dispersions are placed in a prewashed dialysis tubing which can be hermetically sealed [30]. The dialysis sac is then dialyzed against a suitable dissolution medium at room temperature; the samplesarewithdrawnfromthemediumatsuitable intervals,centrifugedandanalyzedfordrugcontent

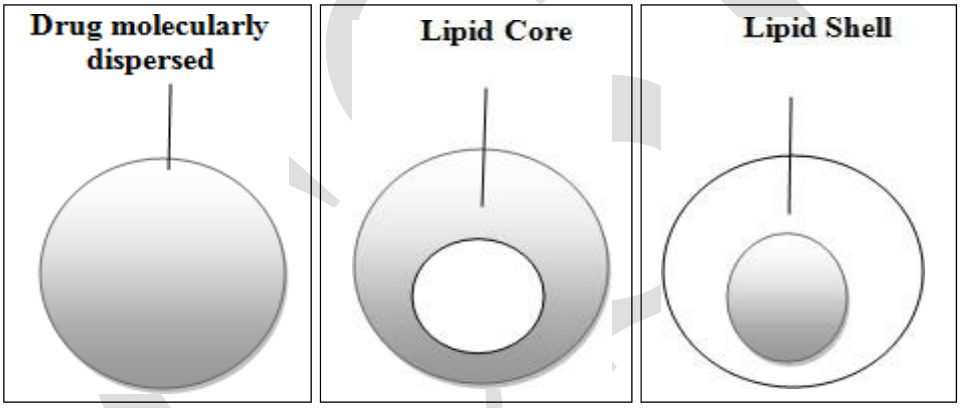
usingasuitablemethod(U.V.spectroscopy,HPLC *etc)*.Themaintenanceof sink condition is essential.

b. Reverse Dialysis: In thistechnique, a number of Small dialysis sac containing 1 ml of dissolution medium are placed in SLN dispersion. The SLNs are then placed into the dissolution medium. The direct dilution of the SLNs is possible with this method; however the rapid release cannot be quantified using this method [30].

c. Franz Diffusion Cell: The SLNs dispersion is placed in the donor chamber of a Franz diffusion cell fitted with a cellophane membrane. The dispersion is then dialyzed against a suitable dissolution medium at room temperature; the samples are withdrawn from the dissolution medium at suitable intervals and analyzed for drug content using a suitable method (U.V.spectroscopy, HPLC *etc*). The maintenance of sink condition is essential.

Drug Release from SLN: Depending upon the drug solubility and drug / lipid ratio, method of preparation, the drug is located in the core of the particles, in the shell or molecularly dispersed throughout the matrix. There are mainly three drug incorporation models which describe the incorporation of drug into SLN.

a. SolidSolutionorHomogenousmatrixmodel.
b. Drugenrichedshell,coreshellmodel.
c. Drugenrichedcore,coreshell model.



a. Solid solution **b. Drug enriched Shell** **c.Drug enriched core**

FIG.3:MODELSOFINCORPORATIONOFACTIVECOMPOUNDSINTOSLN
(a)Homogeneousmatrix,(b)Drugenrichedshellwithlipidcore,(c)Drugenrichedcorewithlipidshell

The above three models are the function of formulation, combination of solid lipid, active ingredients,surfactantsandsometimeco-surfactant andoftheproductiontechniques(hot*vs*.coldhomogenization)

a. Solid Solution Model: In this, the drug is molecularly dispersed in the lipid matrix when the particles are produced by cold homogenization technique and no surfactant or no drug solubilizing surfactant is used. In this, drug has strongly pronounced interactions with the lipid [11,30].

b. Drug Enriched Shell Model: In this model of drug incorporation, a solid lipid core forms when the recrystllization temperature of lipid is reached. On reducing the temperature of this dispersion,drug concentrates in the still liquid outer shell of solid lipid nanoparticles [16].

c. Drug Enriched Core model: In this model of drug incorporation, cooling the nanoemulsion leads to the super saturation of the drug which is dissolved in the lipid and melt at or close to its saturation solubility and the drug participates prior to the lipid recrystallization and finally needs further cooling to the recrystallization of the lipid surrounding the drug as a membrane.

ApplicationsofSLN's

1. Ophthalmic Administration: Many investi-gations have been made to use nanoparticles for prolonged release of drugs to the eye. The basic drawback of ophthalmologic formulation is the fast removal from the eye, which implies clearance of the applied drug through the nose. It could be shown for nanoparticles that an increased adhesiveness is available leading to higher drug levels at desired site of action. However, the basic problem was that the nanoparticles are of limited toxicological acceptance. It was shown by Gasco that SLN have a prolonged retention time at theeye. This was confirmed by using radiolabiled formulations and γ-scintigraphy. The lipids of SLN are easy to metabolize and open a new ways for ophthalmological drug delivery without impairing vision [31].

2. Pulmonary Administration: SLN powders cannot be administered to the lung because the particle size is too small and they will be exhaled.A very simple approach is the aerosolization of aqueous SLN dispersions. The major point is that the SLN should not aggregate during the aerosolization. The aerosol droplets were collected by collision of aerosol with a glass wall of abeaker.ThisbasicallydemonstratesthatSLNare suitable for lung delivery. After localization intothe bronchial tube and in the alveoli, the drug can be released in a controlled way from the lipid particles [32].

3. SLNs as a Targeted Carrier for Solid Tumors: One of the most important challenges in drug delivery is to get the drug at the place it is needed in the body thereby avoiding or reducingthe side effects to non diseased organs. The non restricted toxicity of chemotherapeutics thus limits the full use of their therapeutic potential. Localdrug delivery or drug targeting results in increased local drug concentrations and provides strategiesfor more specific therapy. Nanoparticles have specific particles as tools to enable these strategies. SLNs have been reported to be useful as drug carriers to treat neoplasms [33]. Tumour targeting has been achieved with SLNs loaded with drugs like methotrexate [13], paclitaxel [34] and camptothecin [35].

4. SLNs as Cosmeceuticals: The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers. Cosmeceuticals is rising as the major application target of these carriers. Carrier systems like SLNs and NLC were formulated with a pointof view to meet manufacturing needs like scale up, qualification and validation, simple technology,low cost *etc* [36] The SLNs have been functional in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers [37].

5. SLNs for Liver Targeting: Liver-targeting SLNs with a hepatoprotective drug, cucurbitacin B (Cuc B), using a galactosylated lipid, N-hexadecyl lactobionamide (N-HLBA) was prepared. The galactosyl-lipid N-HLBA was prepared via the lactone form intermediates of lactobionic acid and synthesized by anchoring galactose to hexadecylamine lipid. The Cuc B-loaded galactosylated SLNs and conventional SLNs were successfully prepared by a high - pressure homogenization method.

Theencapsulation ofCucBin SLNs resulted in the improvement of cytotoxic activity and galactosyl ligand could further improve the

cellular accumulation and cytotoxicity of Cuc B. The incorporationofN-HLBAintoSLNsconsiderably improved the liver target ability of Cuc B-loaded SLNs and galactosylated SLN had a great potential as a drug delivery carrier for improved liver target ability.

6. SLNsforPotentialAgricultureApplication: Essentialoilextractedfrom*Artemisiaarborescens* L. when incorporated in SLN, were able to reduce therapidevaporationcomparedwithemulsionsand the systems have been used in agriculture as a suitable carrier of ecologically safe pesticide.

7. Solid Lipid Nanoparticles for Antimicrobial Drug Delivery: Firstly, SLNs contain occlusive excipients that, upon appliance on skin, readily form a thin film to lessen water evaporation and retain skin moisture. SLNs can facilitate the delivery of anti-tuberculosis drugs such asrifampin, Isoniazid and pyrazinamide to the lungs as well as to the lymphatic systems. SLNs can provide a sustained release of the carried antimicrobial payloads, which then can effectively eliminate the infectious microbes harbored at these lymphatic sites. Eventhough the development history of SLN-based antimicrobial drug delivery systems is relativelyshorter than other nanoparticle systems such as liposomes and polymeric nanoparticles, SLNs have shown great therapeutic potentials.

8. SLNs in Breast Cancer and Lymph Node Metastases: Mitoxantrone-loaded SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of drug. Efficacy of doxorubicin (Dox) has been reported to be enhanced by incorporation in SLNs. In the methodology the Dox was complexed with soybean-oil-based anionic polymer and dispersed together with a lipid in water to form Dox-loaded solid lipid nanoparticles. The system has enhanced its efficacy and reduced breast cancer cells.

9. Oral SLNs in Antitubercular Chemotherapy: Antituberculardrugssuchas rifampicin,isoniazide, pyrazinamide-loaded SLN systems were able to reduce the dosing frequency and improve patient compliance. Antitubercular drugs loaded SLNs were prepared using solvent diffusion technique [38].

10. SLNs as Gene Vector Carrier: Cationic solid lipid nanoparticles have established themselves duringthepastdecades.TheycanwellbindDNA directly *via* ionic interaction and intervene gene transfection. SLN can be used in the gene vector formulation [39].

CONCLUSION: SLNs are relatively novel drug deliverysystems, havingreceivedprimaryattention from the early 1990's and future holds great promise for its systematic investigation and exploitation. SLN as colloidal drug carrier combines the advantage of polymeric nano- particles, liposome; like improved physicalstability, feasibility of incorporation of lipophilic and hydrophilic drugs, economic, ease of scale-up, and manufacturing. SLNs can effect site specific and sustained release of drug. SLNs are preparedby various advanced techniques. SLNs have been used extensivelyfor applications in drugdiscovery, drug delivery, and diagnostics and for many others in medical field.

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