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SOLID LIPID NANOPARTICLES FOR ANTIFUNGAL DRUG DELIVERY SYSTEM

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Abstract-**Fungal infections are common throughout much of the natural world. In humans, fungal infections occur when an invading fungus takes over an area of the body and is too much for the immune system to handle. Despite the availability of several effective agents in the antifungal drug, their therapeutic outcome is less than optimal due to limitations related to drug physicochemical properties and toxicity. The improvement of bioavailability of drug is the one greatest challenge in drug formulations. Many commonly used azole antifungal drugs, such as clotrimazole, miconazole, fluconazole, oxiconazole, tioconazole and sertaconazole are hydrophobic and have poor aqueous solubility. To overcome these problems, it is required to develop Lipid based nanocarrier drug delivery systems due to their capacity to increase the solubility. Hence, the purpose of this research is to formulate the well-known antifungal agent loaded SLNs topical cream to improve its efficiency. Solid lipid nanoparticles are at the forefront of the rapidly developing field of nanotechnology with many potential applications in drug delivery, clinical medicine and research, as well as in other varied sciences. Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The ability to incorporate drugs into nanocarriers offers a new prototype in drug delivery that could be used for secondary and tertiary levels of drug targeting. Hence, solid lipid nanoparticles hold great promise for reaching the goal of controlled and site specific drug delivery and hence have attracted wide attention of researchers.**

Key words- **Fungal infections, solid lipid nanoparticles, nanotechnology, efficiency, bioavailability.**

I. INTRODUCTION

The lipids are a large group of organic compounds that has a fundamental role in life on Earth. Whether they act as the energy storage in our bodies or as the building blocks of the cell membranes they play a key role in different physiological and biochemical processes. Due to their intrinsic properties lipids can dissolve water-insoluble substances, pass through biological membranes and undergo digestion by enzymes. In the pharmaceutical industry lipids are used mainly as vehicles in different formulations intended for all routes of administration – as emulsions, ointments, pellets, suppositories etc. The emulsions (type "oil-in-water") are one of the most important systems because they enable the administration of fat-soluble active pharmaceutical ingredients (APIs) throughout various routes.

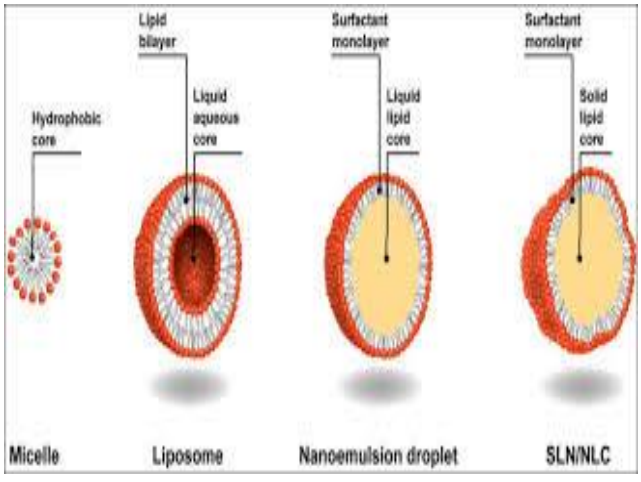

Fig 1: Comparison between micelles, liposomes, nanoemulsions and solid lipid nanoparticles

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The demand to broaden the area of application of oil (lipid) in water dispersions and their continuous optimization resulted in the development of the first solid lipid microparticles in the 1980s by Speiser and coworkers . In the following years, extensive work and experiments with solid lipids resulted in the invention of lipid based solid particles in the submicron range by the groups of Westesen, Müller and Gasco. Solid lipid nanoparticles (SLN) presented in 1991 speak to an optional carrier system to convention colloidal carrier, for example, - emulsions, liposomes and polymeric micro – and nanoparticles. Nanoparticles produced using solid lipids are drawing in significant consideration as novel colloidal medication carrier for intravenous applications as they have been proposed as an option particulate carrier framework. SLN are sub-micron colloidal bearers going from 50 to 1000 nm, which are made out of physiological lipid, scattered in water or in watery surfactant arrangement. SLN offer special properties, for example, little size, vast surface region, high medication stacking and the communication of stages at the interface and are alluring for their potential to enhance execution of pharmaceuticals. Solid lipid nanoparticles are one of the novel potential colloidal transporter frameworks as option materials to polymers which is indistinguishable to oil in water emulsion for parenteral substances. They have numerous focal points, for example, great biocompatibility, low harmfulness and lipophilic medications are better conveyed by robust lipid nanoparticles and the framework is physically steady.

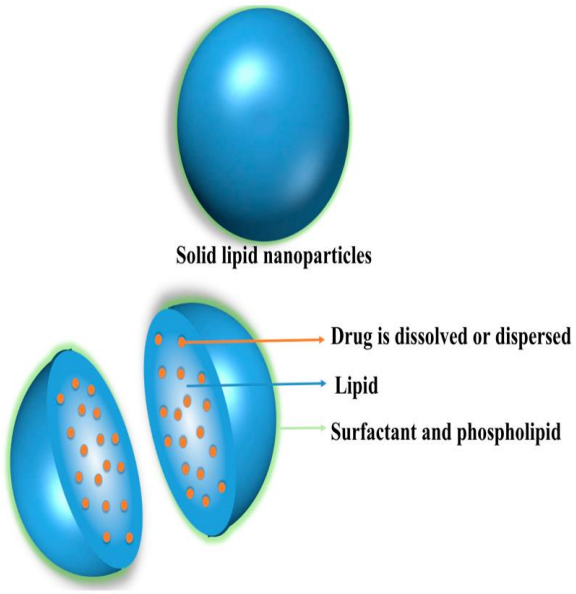

Fig 2: Structure of solid lipid nanoparticles

Table 1: Different SLNs and NLCs formulations used in the delivery of antifungal drugs.

Drug	Lipid formulation	Size (nm)	Drug entrapment efficiency	Reference
Itraconazole	NLCs	314	70.5±0.6%	Lim et al.(2014)[1]
Itraconazole	NLCs	102-106	99.98%	Pardeike et al. (2016)[2]
Itraconazole	NLCs	131-132	ND	Pardeike et al. (2012)[3]
Itraconazole	NLCs	114	98.78%	Pardeike et al. (2011)[4]
Itraconazole	SLNs	250-545	81-88%	Mirza et al. (2016)[5]
Itraconazole	SLNs	126-199	68-94%	Mohanty et al.(2015)[6]
Itraconazole	NLCs	192-240	83-95%	Kim et al.(2010)[7]
Fluconazole	SLNs	85	89.60%	Moazeni et al.(2015)[8]
Fluconazole	SLNs	178	75.70%	Gupta and Vyas (2012)[9]
Fluconazole	NLCs	134	81.40%	Gupta and Vyas (2012)[9]
Fluconazole	SLNs	179-279	50-75%	Gupta et al. (2013)[10]

Miconazole	SLNs	206	90.80%	Jain et al. (2010)[11]
Miconazole	SLNs	23	90.20%	Aljaeid and Hosny (2016)[12]
Miconazole	SLNs	244-766	80-100%	Bhalekar et al. (2009)[13]
Miconazole	NLCs	54	86.77%	Singh et al. (2013)[14]
Miconazole	NLCs	213-231	87%	Mendes et al. (2013)[15]
Clotrimazole	SLNs and NLCs	<300	65-70%	Souto et al. (2004)[16]
Clotrimazole	SLNs	50-150	82-87%	Das et al. (2012)[17]
Clotrimazole	NLCs	50-150	85-89%	Das et al. (2012)[17]
Clotrimazole	NLCs	202	97%	Esposito et al. (2013)[18]
Clotrimazole	SLNs	120	87%	Das et al. (2014)[19]
Clotrimazole	NLCs	160	88%	Das et al. (2014)[19]
Clotrimazole	SLNs	202-460	41-43%	Cassano et al. (2016)[20]
Ketoconazole	SLNs	202-460	33-36%	Cassano et al. (2016)[20]
Griseofulvin	SLNs	117	66%	Aggarwal and Goindi (2013)[21]
Terbinafine	SLNs	300	73.74%	Vaghasiya et al. (2013)[22]
Terbinafine	SLNs	80-200	ND	Chen et al. (2012a)[23]
Voriconazole	SLNs	234-343	62-84%	Khare et al. (2016)[24]
Voriconazole	SLNs	139-334	40-64%	Kumar and Sinha (2016)[25]
Voriconazole	NLCs	250	75%	Andrade et al. (2016)[26]
Voriconazole	NLCs	210	86%	Song et al. (2014)[27]
Econazole	SLNs	150	100%	Sanna et al. (2007)[28]

II. ADVANTAGES OF SOLID LIPID NANOPARTICLES

1. Excellent biocompatibility.
2. No special solvent required.
3. Long term stability.
4. Possibility of controlled drug release and drug targeting.
5. Large scale production.
6. Reduces the no. of doses required.
7. Easy to manufacture.
8. High drug pay load.
9. Application versatility.

III. DISADVANTAGES OF SOLID LIPID NANOPARTICLES

1. Poor drug loading capacity.
2. Drug expulsion after polymeric transition during storage.
3. Relatively high water content of the dispersions.
4. Particle growth.
5. Unpredictable gelation tendency.

IV. PRINCIPLE OF DRUG RELEASE FROM SLN

The general standards of medication discharge from lipid nanoparticles are as per the following:

1. Higher surface territory because of little molecule measure in nanometer extent gives higher medication discharge.

2. Slow medication discharge can be accomplished when the medication is homogenously scattered in the lipid framework. It depends on sort and medication entanglement model of SLN.

3. Crystallization conduct of the lipid carrier and high portability of the medication lead to quick medication discharge.

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4. Fast initial drug release in the first 5 min in the drug –enriched shell model as a result of the outer layer of particle due to larger surface area of drug depositon on the particle surface.

5. The burst release is reduced with increasing particle size and prolonged release could be obtained when the particles were sufficiently large, i.e., lipid macromolecules.

6. The type of surfactant and its concentration, which will interact with the outer shell and affect its structure, should be noted as the outer factor which is important, because a low surfactant concentration leads to a minimal burst and prolonged drug release.

7. The particle size affect drug release rate directly depends on various parameters such as composition of SLN formulation (such as surfactant, structural properties of lipid, drug) production method and conditions (such as production time, equipment, sterilization and lyophilization.

V. DRUG INCORPORATION MODELS OF SLN29

a) Homogenous matrix model
b) Drug enriched shell with lipid core
c) Drug enriched core with lipid shell

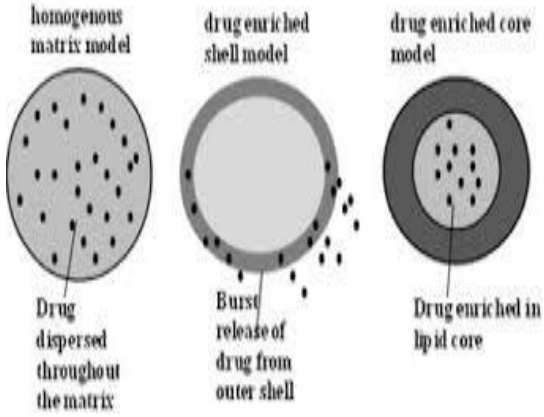

Fig 3: Drug incorporation

Solid solution model	**Core-shell model (drug-enriched shell)**	**Core-shell model (enriched core)**
Formation of this model in cold homogenization technique.	Formation of this model in hot homogenization technique.	Dispersion cooling leads to a super saturation of the drug which is dissolved in the lipid.
Using no drug-solubilizing Surfactant	Formation of lipid core at recrystallization temperature of lipid	Precipitation of drug in melted lipid
Drug dispersed in lipid matrix.	Cooling of the obtained dispersion leads to repartitioning of the drug to the lipid phase.	Finally, further cooling lead to recrystallization of the lipid.
There is a strong interaction between lipid and drug.	Concentration of drug in surrounding membrane.	Formation of drug-enriched core.

A. Factors affecting loading capacity of a drug in lipid are:

1. Solubility of drug in lipid melt.
2. Miscibility of drug melt and lipid melt.
3. Chemical and physical structure of solid matrix lipid.
4. Polymorphic state of lipid material.

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VI. COMPOSITION OF SLNS[29]

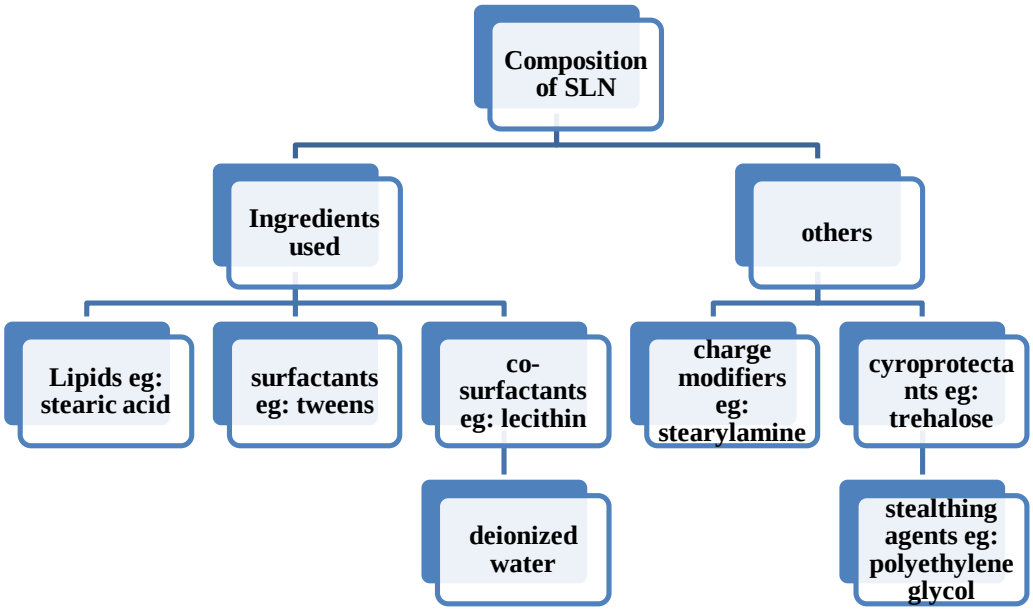

Fig 4: Composition of SLN

i. LIPIDS:

The lipid, itself, is the main ingredient of lipid nanoparticles that influence their drug loading capacity, their stability and the sustained release behavior of the formulations.

ii. *Selection criteria for lipids:*

Important point to be considered in the selection of drug carrier system (lipid) is its loading capacity and also the intended use.

1. Lipids that form highly crystalline particles with a perfect lattice cause drug expulsion.
2. More complex lipids containing fatty acids of different chain length form less perfect crystals with many imperfections. These imperfections provide the space to ac
3. commodate the drugs.

iii. *Role of emulsifier:*

1. Provide adequate stability to the preaparation by covering the surface of nanoparticles.
2. To avoid this co-emulsifiers are employed.

iv. *Role of Co-emulsifier:*

1. Due to low mobility of the phospholipid molecules, sudden lack of emulsifier on the surface of the particle leads the particle aggregation and increase in the particle size of SLNs.
2. To avoid this co-emulsifiers are employed

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v. ***Other ingredients:***

Cryoprotectants	Trehalose, mannose mannitol, polyvinyl, pyrolidone, glucose, maltose, lactose, glycine, gelatin, etc.
Charge modifiers	Stearylamine, diacetyl phosphate, dipalmitoyl phosphatidyl choline (DPPC), dimyristoyl phosphatidyl glycerol (DMPG)
Stealthing agents (agents for improving circulation time)	Poloxamer, polyethylene glycol

VII. PREPARATION OF SOLID LIPID NANOPARTICLES [29]

The performance of SLNs greatly depends on the method of preparation which in turn influences the particle size, drug loading capacity, drug release, drug stability etc. Different approaches exist for the production of finely dispersed lipid nanoparticle dispersions.

i. High pressure homogenization
   a) Hot homogenization
   b) Cold homogenization
ii. Ultrasonication/high speed homogenization
   a) Probe ultrasonication
   b) Bath ultrasonication
iii. Solvent emulsification-evaporation method
iv. Supercritical fluid method
v. Microemulsion based method
vi. Spray drying method
vii. Double emulsion method
viii. Precipitation technique
ix. Film-ultrasound dispersion

i. High pressure homogenization[29]:

HPH is a reliable and suitable method for the preparation of SLN, NLC and LDC and can be performed at elevated temperature (hot HPH technique) or at or below room temperature (cold HPH technique). SLNs made from solid lipids or lipid blends produced by high pressure homogenization of melted lipids disperse in an aqueous as outer phase stabilized by surfactant as tween80, SDS, lecithin etc.

- High pressure homogenization pushes a liquid with high pressure (100-2000 bar) through a narrow gap.
- The fluid accelerate on a very short distance to very high velocity(over 100 km / hr)
- Very high shear stress and cavitation forces disrupt the particles down to the submicron range.
- Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated.

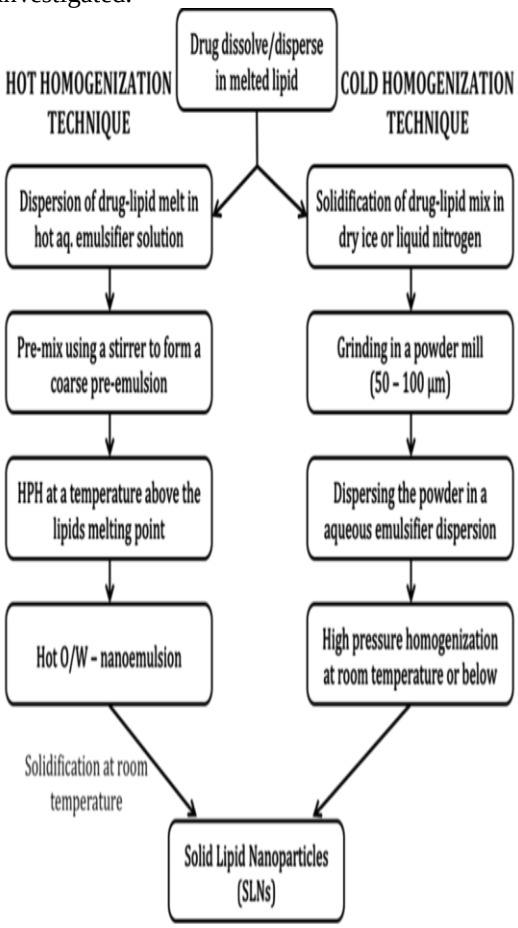

Fig 5: Hot homogenization and Cold homogenization

Advantages

- Low capital cost.
- Demonstrated at lab scale.

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Disadvantages

- Energy intensive process.
- Polydisperse distributions.
- Unproven scalability.

ii. Ultrasonication or high speed homogenization[30]:

This ultrasonication technique is a dispersing technique, which was initially used for the production of solid lipid nanodispersion. Ultrasonication based on the mechanism of cavitation. In first step, the drug was added to previously melt solid lipid. In second step, the heated aqueous phase (heated to same temperature) was added to the melted lipid and emulsified by probe sonication or by using high speed stirrer or aqueous phase added to lipid phase drop by drop followed by magnetic stirring. The obtained pre-emulsion was ultrasonicated using probe sonicator with water bath (at 0ºC). In order to prevent recrystalization during the process, the production temperature kept at least 5ºC above the lipid melting point. The obtained nanoemulsion (o/w) was filtered through a 0.45µm membrane in order to remove impurities carried in during ultrasonication. Then they obtained SLN is stored at 4ºC. To increase the stability of the formulation, was lyophilized by a lyophilizer to obtain freeze-dried powder and sometime mannitol (5%) was added into SLNs as cryoprotector.

Advantages:

- Reduced shear stress.

Disadvantages:

- Potential metal contamination.
- Physical instability like particle growth upon storage.

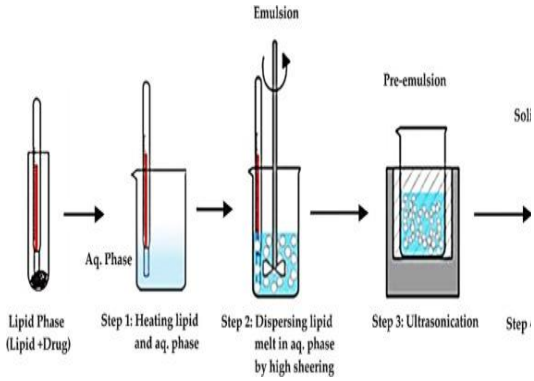

Fig 6: Ultrasonication

iii. Solvent emulsification evaporation method

Solvent emulsification evaporation method (SEE) has three basic steps for preparation of nanoparticles. In step (I), lipid material is added to a known volume of organic solvent and mixed properly to yield a homogenous clear solution of lipid. In step (II), above prepared solution is added to the right volume of water in order to form a coarse emulsion by using high-speed homogenizer. Nanoemulsion is then obtained in step (III) by using high-pressure homogenizer, which convert the coarse emulsion into a nanoemulsion due to high pressure, resulting in breakdown of the globules. After nanoemulsion formation, it is kept overnight under continuous stirring on a magnetic stirrer or kept in a hood to remove the traces of organic solvent. Nanodispersion is formed after evaporation of organic solvent, as lipid material will precipitate in the water. The precipitation of lipids in aqueous medium is separated out by filtering through sintered disc filter funnel. Nanoparticles prepared by this strategy are nanosized, non-flocculated (single entity) and have high entrapment efficiency.

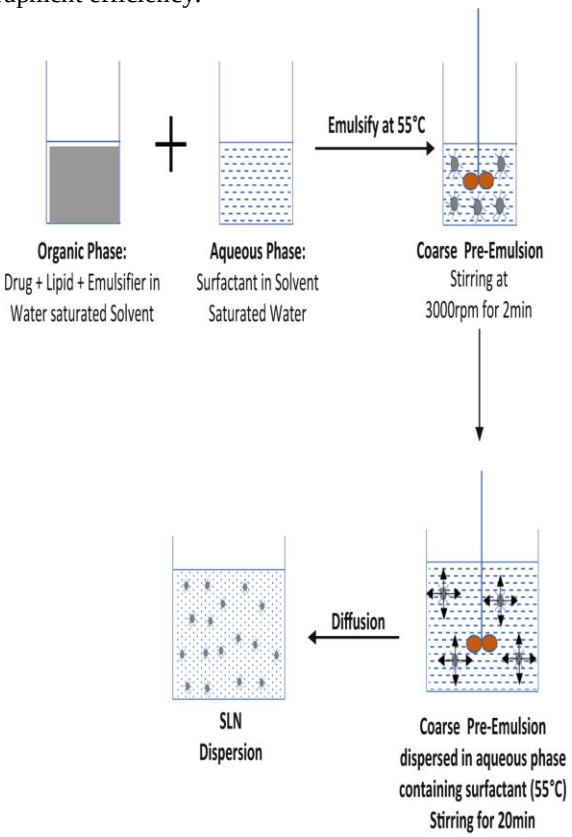

Fig 7: Solvent emulsification evaporation method

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iv. Super critical fluid method

In this method, SLNs are prepared by particles from gas saturated solutions (GSS), thereby providing the advantage of solvent-less processing. SLN can be organized by using the fast expansion of supercritical carbon dioxide solutions. GSS helps in melting the lipid material, whereafter the lipid melt along with GSS will dissolve in the super critical fluid (SCF) under pressure. The saturated solution is sprayed through the nozzle or atomizer, which causes the expansion of solution whereby SCF escapes rapidly leaving behind the fine dry lipid particles. Absence of organic solvents and wide range miscibility of lipids in SCF justify the advantage of this technique.

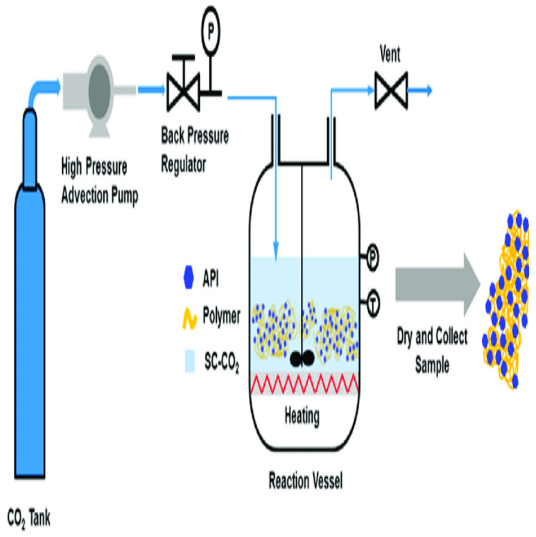

Fig 8: Super critical fluid method

v. Microemulsion based method

This technique involves dilution of a microemulsion to precipitate the lipid. SLNs are produced by stirring an optically transparent mixture containing a low melting fatty acid, an emulsifier, coemulsifiers and water at 65–70 °C. After that, the hot microemulsion is dispersed in cold water under stirring. The volume ratios of the hot microemulsion to cold water usually are in the range of 1:25 to 1:50. The dilution process is critically determined by the composition of the microemulsion. This microemulsion is then dispersed in a cold aqueous medium under mild mechanical mixing, which leads to precipitation of the lipid phase in to SLNs.

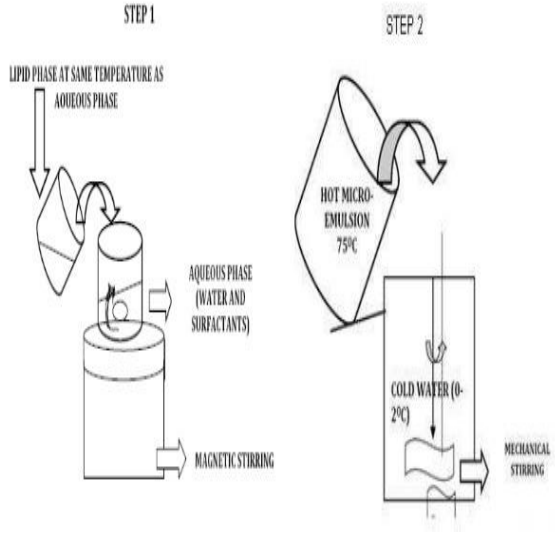

Fig 8: Microemulsion based method

vi. Spray drying method

Spray Drying Method The spray drying method is an alternative procedure to transform an aqueous SLN dispersion into a drug product. This method is barely used for formulation of SLNs; however, it is cheaper than lyophilization. Particle aggregation due to high temperature and shear force, and partial melting of the particles are drawbacks associated with this method. This method requires lipid that have a melting point above 70˚C.

vii. Double emulsion method

Double emulsion technique is one of the most frequently used techniques to prepare nanoparticles encapsulated with hydrophilic drugs using stabilizer or surface-active agent. This method is also known as multiple emulsion method, where it has three basic steps: (i) formation of the water in oil emulsion or inverse emulsion, (ii) addition of the W1/O emulsion into the aqueous solution of polymer or surfactant to form a W1/O/W2 emulsion with continuous stirring (sonication or homogenization), and (iii) evaporation of the solvent or filtration of the multiple emulsion to form the nanoparticles. The double emulsion technique produces larger sized particles, than surface modification is achievable through this technique by incorporating hydrophilic polymers such as PEG during step ii.

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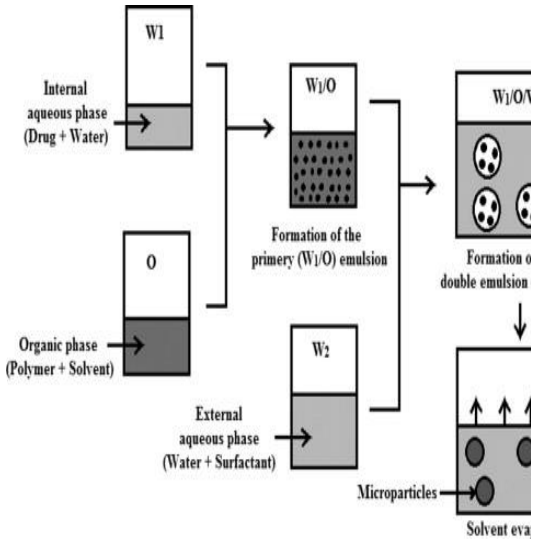

Fig 9: Double emulsion method

viii. 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 in an organic solvent (e.g. chloroform) and the solution will be emulsified in an aqueous phase. After evaporation of the organic solvent the lipid will be precipitated forming nanoparticles.

ix. Film-ultrasound dispersion

The lipid and the drug were put into suitable organic solutions, after decompression, rotation and evaporation of the organic solutions, a lipid film is formed, then the aqueous solution which includes the emulsions was added. Using the ultrasound with the probe to diffuser at last, the SLN with the little and uniform particle size is formed.

VIII. OPTIMIZATION[31]

- Optimization of Process Variables**:** On the basis of literature survey and a few trial batches, various critical process variables which may have significant effect on the critical quality attributes were identified for each step involved in the formulation and were subjected to optimization. Preliminary optimization of stirring time, RPM, and temperature was done by conducting the experiments at three levels of each process variables involved during stirring of the hot aqueous surfactant solution while adding the drug incorporated lipidic phase for the formation of coarse emulsion. Critical process variables involved during the high pressure homogenization were optimized using 3^2 factorial design with Design Expert 9.0.3.1 software (Stat-Ease, Inc., USA). The pressure and number of cycles were selected as independent variables and the response on particle size and PDI were investigated.
- Optimization of Formulation Variables : 3^2 factorial design was employed for optimization of formulation variables and Design Expert 9.0.3.1 software was used for statistical analysis by ANOVA, generating model equations and constructing contour plots and 3D surface plots for each response. Amount of drug with respect to lipid and concentration of surfactant were investigated as independent variables at three levels and the critical quality attributes selected were particle size, PDI, and entrapment efficiency as responses.

IX. CHARACTERIZATION PARAMETERS

i. Particle Size and Shape

SLNs are submicron sized, particle size and shape is determined by**:**

ii. Photon Correlation Spectroscopy (PCS)

It is an established method which is based on dynamic scattering of laser light due to Brownian motion of particles in solution/suspension. This method is suitable for the measurement of particles in the range of 3 nm to 3 mm. The PCS device consists of laser source, a sample cell (temperature controlled) and a detector. Photomultiplier is used as detector to detect the scattered light. The PCS diameter is based on the intensity of the light scattering from the particles.

iii. Electron Microscopy

Electron Microscopy methods such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are used to measure the physical characterization like overall shape and morphology of lipid nanoparticles. It permits the determination of particle size and distributions. SEM uses electrons transmitted from the surface of the sample while TEM uses electrons transmitted through the sample. TEM has a smaller size limit of detection**.**

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iv. Measurement of zeta potential

Zeta potential is used to measure the charge on the particles. It allows prediction about the storage stability of colloidal dispersion because of repulsion between particles. Malvern Zetasizer is most widely used instrument for measurement of Zeta potential. A zeta potential measurement can also be helpful in designing particles with reduced RES uptake. Zeta potential below -25 mV and above + 25mV are required for full electrostatic stabilization of the formulation.

v. Determination of Incorporated Drug

Amount of drug incorporated in SLNs influences the release characteristics; hence it is very important to measure the amount of incorporated drug. The amount of drug encapsulated per unit weight of nanoparticles is determined after separation of the free drug and solid lipids from the aqueous medium by ultracentrifugation, centrifugation filtration or gel permeation chromatography. The drug can be assayed by standard analytical technique such as spectroscopy and HPLC methods.

vi. Storage stability of SLN

The physical properties of SLN's during prolonged storage can be determined by monitoring changes in zeta potential, particle size, drug content, appearance and viscosity as the function of time. External parameters such as temperature and light appear to be of primary importance for long term stability. The zeta potential should be in between -100 to + 100 mV for a dispersion to remain physically stable.
4°C - Most favorable storage temperature.
20°C - Long term storage did not result in drug loaded SLN aggregation or loss of drug.
50°C - A rapid growth of particle size is observed.

X. EVALUATION PARAMETERS

Various methods used to study the in vitro release of the drug are:

i. In vitro drug release[29]

Franz Diffusion Cell:

The SLN's dispersion is placed in the donor chamber of Franz diffusion cell fitted with a cellophane membrane. The dispersion is then analyzed against a suitable dissolution medium; the samples are withdrawn from the dissolution medium at suitable intervals and analyzed for drug content using suitable methods like spectroscopy and HPLC methods.

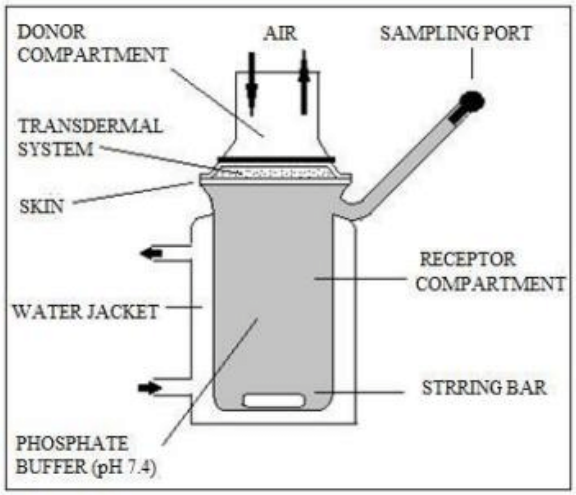

Fig 10: Franz diffusion cell assembly

XI. APPLICATIONS

i. SLN for Topical application

SLN and NLC are very attractive colloidal carrier systems for skin applications due to their various desirable effects on skin besides the characteristics of a colloidal carrier system. During the last few years, SLN and NLC have been studied with active compounds such as Vitamin E, tocopherol acetate, retinol, ascorbyl palmitate, clotrimazole, triptolide, phodphyllotoxin and a nonsteroidal antiandrogen RU 58841 for topical application.

ii. 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. The *in vivo* study showed that skin hydration will be increased by 31% after 4 weeks by addition of 4% SLN to a conventional cream. SLN and NLCs have proved be controlled release innovative occlusive topicals.

iii. SLN for Respiratory Application[33]:

The lungs offer a high surface area for drug absorption by avoiding first-pass effects. Rapid drug absorption by aerosolization of drugs (in the 1-3 μm size range) occurs since the walls of alveoli in the deep lung are extremely thin. Lymphatic drainage plays an important role in the uptake of particulates in the respiratory system. SLN can be proposed as

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carriers of anticancer drugs in lung cancer treatment or peptide drugs to improve their bioavailability. Assessment of inhaled radio-labeled SLN bio distribution has been described and the data showed an important and significant uptake of the radio-labeled SLN into the lymphatic after inhalation. In a recent study, antitubercular drugs (rifampicin, isoniazid and pyrazinamide) were incorporated into various formulations of solid lipid particles ranged from 1.1-2.1 μm and formulations were nebulized to guinea pigs by mouth for direct pulmonary delivery. Nebulization of solid lipid particles carrying antitubercular drugs was observed to be successful in improving drug bioavailability and reducing the dosing frequency for better management of pulmonary tuberculosis.

iv. Solid Lipid Nanoparticles in Cancer Chemotherapy[29]

Outcomes of these studies have been shown to improve the efficacy of chemotherapeutic drugs, simultaneously reduction in side effects associated with them. Improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, enhanced drug efficacy, improved pharmacokinetics and less in vitro toxicity are the important features of SLN which make them a suitable carrier for delivering chemotherapeutic drugs. Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cells, are at least partially overcome by delivering the musing SLN.

v. SLN as Potential new Adjuvant for Vaccines

Adjuvants are used in vaccination to enhance the immune response. The safer new subunit vaccines are less effective in immunization and therefore effective adjuvants are required. New developments in the adjuvant area are the emulsion systems. These are oil-in-water emulsions that degrade rapidly in the body.

XII. SUMMARY AND CONCLUSION

Solid lipid nanoparticle drug delivery technology presents considerable opportunities for improving medical therapeutics, but the technology's potential remains unrealized. Clear advantages of SLN include the composition, the rapid and effective production process including the possibility of large scale production and the possibility to produce carriers with higher encapsulation efficiency. But the major problem of SLNs is the low capacity to load hydrophilic drugs due to partitioning effects during the production process. The improvement of bioavailability of drug is the one greatest challenge in drug formulations. Many commonly used azole antifungal drugs, such as clotrimazole, miconazole, fluconazole, oxiconazole, tioconazole and sertaconazole are hydrophobic and have poor aqueous solubility. To overcome these problems, it is required to develop Lipid based nanocarrier drug delivery systems due to their capacity to increase the solubility.

XIII. FUTURE ASPECTS

In this review, we tried to give an insight of the most of the reported studies that make use of SLNs for their treatment, during the last few years. We have described a variety of fabrication and characterization techniques for the synthesis of the solid lipid nanoparticles. SLNs exhibited improved skin penetration due to enhanced contact between drug and skin resulting from the large particle surface area and film formation. Consequently, future work on the prepared SLN would be promising with respect to evaluation of effectiveness as prophylactic treatment as well as detailed regimen (dose and duration) study which will be the forefront of our laboratory in order to be transformed into potential marketed product. Preparations which are already present in market have low bioavailability. SLNs are submicron colloidal carriers ranging from 50 to 1000nm because of their particle size they easily penetrates into the skin, which increases its bioavailability.

XIV. REFERENCES

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