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Solid lipid nanoparticles; as a promising drug delivery method to get greater bioavailability: A review

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Abstract

Solid lipid nanoparticles (SLN) are the heart of nanotechnology's tremendous development, with multiple practical benefits in drug delivery and research. Because of their size-dependent properties, solid Lipid nanoparticles can be used to create innovative medicines. Drug conversion into nanoparticles provides a new drug delivery concept that could be used for drug targeting. As a result, solid lipid nanoparticles have great promise reaching the goal of targeted and site-specific drug delivery. The goals, production techniques, advantages, limits are all discussed in this review. Scanning electron microscopy and measurement of particle size and zeta potential, dynamic light scattering are examples of appropriate analytical techniques for SLN characterization. By using novel drug formulation technologies, the drug delivery system focuses on the regulation of in vivo dynamics in order to enhance the efficacy and safety of the included pharmaceuticals. Lipids used in the development of Nano particulate dosage forms, such as fatty acids, triglycerides, vegetable oils, and their derivatives. Solid lipid nanoparticles (SLNs) are a type of lipid drug delivery method that is relatively new. They were created to solve some of the limitations with traditional drug delivery systems, such as low drug encapsulation efficiency and limited bioavailability of Biopharmaceutical Classification Systems (BCS) class II and IV medications. SLNs are made up of physiologically well tolerated substances and melt-emulsified lipids that are solid at room temperature that helps to enhance drug bioavailability ultimately results in better desired therapeutic effect.

Keywords: SLNs; BCS class II; Targeted drug delivery; Zeta potential; Ultra-sonication

1. Introduction

Solid lipid nanoparticles (SLNs) are generally known as lipid nanoparticles (LNPs).SLNs are lipid-based nanoparticles. They are an innovative pharmaceutical drug delivery method as well as a new pharmaceutical formulation (1).

Solid lipid nanoparticles (SLN) were first introduced in 1991 as an alternative to traditional colloidal carriers like emulsions, liposomes, and polymeric micro and nanoparticles. As an alternate particulate carrier system, nanoparticles produced from solid lipids are getting a lot of attention as a new colloidal drug carrier for intravenous applications.

SLNs are sub-micron colloidal carriers with diameters ranging from 50 to 1000 nm, made up of physiological lipid and dispersed in water or an aqueous surfactant solution. SLN are appealing for their potential to increase pharmaceutical efficacy due to their unique qualities such as tiny size, vast surface area, high drug loading, and phase interaction at the interface.

Solid lipid nanoparticles are an innovative possible colloidal carrier system as an alternative to polymers that is identical to oil in water emulsion. The liquid lipid has been replaced with a solid lipid.

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Solid lipid nanoparticles (SLNs) have been considered the most effective lipid-based colloidal carriers. This is one of the most used methods for increasing the oral bioavailability of medicines that are poorly water soluble. SLNs are made up of physiologically acceptable lipid components that are solid at room temperature and are in the submicron size range of 50-1000 nm. All of the benefits of polymeric nanoparticles, fat emulsions, and liposomes are combined in SLNs.

SLNs have many benefits, including superior biocompatibility, minimal toxicity, and improved delivery of lipophilic medicines via solid lipid nanoparticles, as well as a physically stable system (2).

Solid lipid nanoparticles (SLNs) have a huge amount of potential in terms of achieving the goal of site-specific drug delivery. SLNs are at the forefront of innovation of the rapidly evolving field of Nano pharmaceuticals, with a variety of possible uses in drug delivery, clinical treatment, and research.

In pharmaceutics, SLNs have gained worldwide recognition as a replacement for liposomes and polymeric nanoparticles. SLNs have strong tolerance and stability. Poorly soluble medications can be included into SLN to improve gastrointestinal solubilization, absorption, and bioavailability.

Good biocompatibility, lesser cytotoxicity, drug targeting, good production scalability, modification of drug release, avoidance of organic solvents in the preparation process, and a broad potential application spectrum are the significant benefits of SLN over other standard drug carriers (oral, dermal, intravenous etc.). Furthermore, increased bioavailability and environmental protection of sensitive active compounds have been observed.

Another main aspect of SLN formulations is their capacity to be stable for several years, which is critical for colloidal drug carriers, and they can be lyophilized or steam sterilized. The attempts of pharmaceutical companies to develop commercially viable drugs using their own technologies demonstrate the promise of these SLNs.

SLNs have a high specific surface area due to their small diameters, a spherical shape and frequently favorable zeta potential. Some other peculiarities of SLNs include the pro longed release obtained in vitro for drugs incorporated in SLN, their rapid uptake (internalization) by cell lines (5-10min), and the possibility to prepare stealth SLNs so as to avoid the reticulo-endothelial system (3).

Solid lipid nanoparticles (SLN) based on pure triglycerides like tripalmitate exhibit limited drug payloads and drug expulsion from the crystal lattice (9). Using complex glycerides like hard fats as a matrix for SLN, incorporation of lipophilic drugs is facilitated, However, these hard fat SLN stead of solid particles (4).

The goal of this review is to create solid lipid nanoparticles, lipid-based drug carrier with higher payloads and controlled release characteristics. This was accomplished by including oils containing triglycerides in the solid core of the particles.

Solid lipids are not only found in semi-synthetic materials, but also in naturally occurring goods such as milk, cream, and cocoa butter. Similarly, liquid ails were supplemented with traditional SLN in this investigation. Our idea is to create a carrier with a solid matrix but liquid domains, combining the benefits of the solid matrix, which limits drug leakage, with the advantages of the liquid regions, which have comparable high lipophilic drug solubility. Unlike the hard fats, a bulk substance with a sufficiently high melting point (70°C) was selected.

Goals of solid lipid nanoparticles: (2) (6).

- To get maximum drug bioavailability.
- Tissue targeting.
- Good patient compliance.
- Controlled drug release is a possible.
- Ability to deliver traditionally difficult drugs such as lipophiles, amphiphiles, biomolecules.
- Stability of the drug has improved.
- Payload of drugs is high.
- The carrier has no bio- toxicity.
- Organic solvents should be avoided.
- Drugs that are lipophilic and hydrophilic are combined.

Advantages of SLNs: (2).

- Stability is extremely high.
- Control and/or target the release of drugs.
- Biocompatibility is excellent.
- Improve pharmaceutical stability.
- Drug content is high and improved.
- Scaling and sterilization are simple.
- Polymeric chemical release kinetics can be effectively controlled.
- Lipidic bioactive chemicals have a higher bioavailability.
- Chemical protection for integrated labile chemicals
- Biopolymeric nanoparticles are far more difficult to make.
- There is no need for a particular solvent.
- Emulsions can be made using conventional technology.
- The same raw components are required for emulsions.
- Long-term use.
- Variability in application.
- Commercial sterilization treatments are possible.

Limitations: (2).

- Particle growth.
- Unpredictable gelation tendency.
- Unexpected dynamics of polymeric transitions.

2. Methods of preparation of SLNs:

SLNs are prepared from lipid, emulsifier and water solvent by using different methods and are

- High pressure homogenization
  - Hot homogenization
  - Cold homogenization
- Ultra- sonication high speed homogenization
  - Probe ultra- sonication
  - Bath ultra-sonication
- Solvent evaporation method
- Solvent emulsification-diffusion method
- Supercritical fluid method
- Micro-emulsion based method
- Spray drying method
- Double emulsion method
- Precipitation technique
- Film-ultrasound dispersion

2.1. High pressure homogenization (HPH):

It is a reliable and powerful technique, which is used for the production of SLNs. High pressure homogenizers push a liquid with high pressure (100-2000 bar) through a narrow gap (in the range of a few microns. The fluid accelerates on a very short distance to very high velocity (over 1000 Km/h). 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.

Two general approaches of HPH are hot homogenization and cold homogenization; work on the same concept of mixing the drug in bulk of lipid melt.

2.1.1. Hot homogenization

Hot homogenization is carried out at temperatures above the melting point of the lipid and can therefore be regarded as the homogenization of an emulsion. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifier phase (same temperature) is obtained by high-shear mixing device HPH of the pre-emulsion is carried out at temperatures above the melting point of the lipid. In general, higher temperatures result in lower particle sizes due to the decreased viscosity of the inner phase However, high temperatures increase the degradation rate of the drug and the carrier. Increasing the homogenization pressure or the number of cycles often results in an increase of the particle size due to high kinetic energy of the particles.

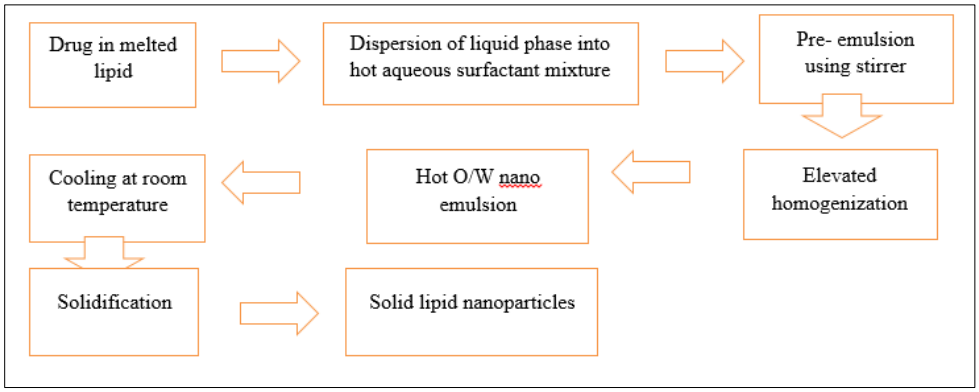

Figure 1 Hot Homogenization

2.1.2. Cold homogenization:

Cold homogenization was designed to eliminate a number of issues associated with homogenization, including temperature-induced drug degradation, drug distribution into the aqueous phase during homogenization, and the complexity of the Nano emulsion crystallization step, which leads to modifications and/or super cooled melts. In this method, a drug containing lipid melt is cooled to form lipid micro particles, which are then dispersed in a cold surfactant to produce a pre-suspension. After homogenizing the pre-suspension at or below room temperature, the gravitational force is powerful enough to breakdown the lipid micro particles directly into solid lipid nanoparticles

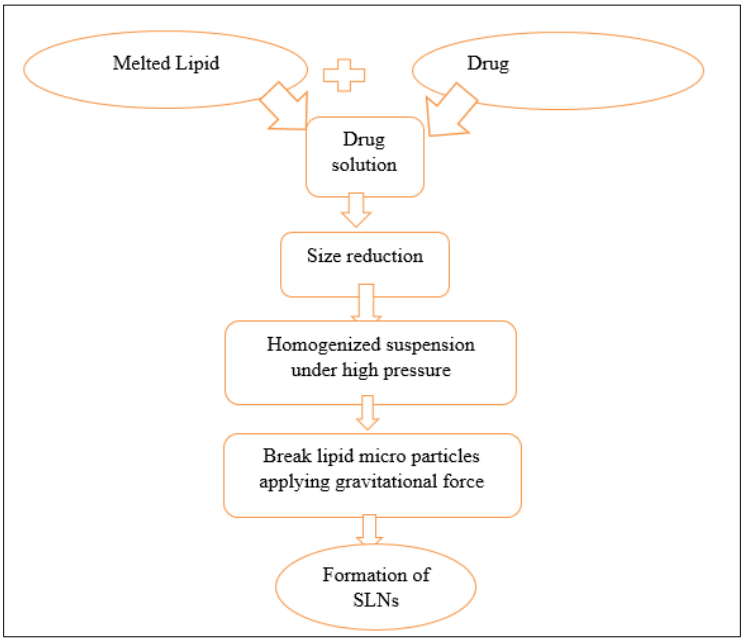

Figure 2 Cold Homogenization

2.2. Ultra sonication/high speed homogenization:

SLNs are also prepared by ultra-sonication or high speed homogenization techniques. For smaller particle size combination of both ultra-sonication and high speed homogenization is required.

2.3. Solvent evaporation

SLNs can also prepared by solvent evaporation method The lipophilic material is dissolved in a wet immiscible organic solvent (e.g. cyclohexane) that is emulsified in an aqueous phase Upon evaporation of the solvent nanoparticles dispersion is formed b. precipitation of the lipid in the aqueous medium by giving the nanoparticles of 25 nm mean sure. The solation was emulsified in an aqueous phase by high pressure homogenization. The organic solvent was removed from the emulsion by evaporation under reduced pressure (40-60 mbar).

2.4. Micro-emulsion based method

This method is based on the dilution of micro emulsions. As micro-emulsions are two-phase systems composed of an inner and outer phase (e. g o/w micro emulsions). They are made by stirring an optically transparent mixture at 65-70°C, which typically composed of a low melting fatty acid (e. g. stearic acid), an emulsifier (e.g. polysorbate 20), co-emulsifiers (e.g. butanol) and water. The hot micro emulsion is dispersed in cold water (2-3 ℃) under stirring. SLN dispersion can be used as granulation fluid for transferring in to solid product (tablets, pellets) by granulation process, but in case of low particle content too much of water needs to be removed High-temperature gradients facilitate rapid lipid crystallization and prevent aggregation. Due to the dilution step, achievable lipid contents are considerably lower compared with the HPH based formulations.

2.5. Spray drying method

It is an alternative technique to the lyophilization process. This recommends the use of lipid with melting point more than 70°C The best results were obtained with SL N concentration of 1^ 3 in a solution of trehalose in water or 20% trehalose in ethanol-water mixture .

2.6. Double emulsion method:

Here the drug is encapsulated with a stabilizer to prevent the partitioning of drug in to external water phase during solvent evaporation in the external water phase of w/o/w double emulsion.

2.7. Precipitation method

The glycerides are 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.

2.8. 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.

2.9. Need for SLNs

The major needs in the design of solid lipid nanoparticles such as a delivery system to control particle size, surface structures, and the release of pharmaceutical agents to achieve a specific drug action a reasonable rate and dose. Polymeric nanoparticles provide certain advantages over liposomes. For example, they help increase drug/protein stability and possess useful nanospheres controlled release properties (5).

2.10. General overview of SLNs

For lipid and lipid-based drug delivery systems, phospholipids are an important constituent because of their various properties, such as amphiphilic nature, biocompatibility and multifunctionality. However, liposomes, lipospheres, and micro-emulsion carrier systems have many drawbacks such as their complicated production method, low percentage entrapment efficiency (% EE), difficult large-scale manufacture, and thus the SLN delivery system has emerged. SLNs are commonly spherical in shape with a diameter in the range of 50 to 1000 nm. The key ingredients of SLN formulations include lipids, which are in the solid state at room temperature, emulsifiers and sometimes a mixture of both, active pharmaceutical ingredients (APIs) and an adequate solvent system Nano carrier-based drug delivery systems can be subcategorized in many aspects depending on the route of administration, degree of degradability, etc. The route of

administration includes nanoparticles for parenteral administration, oral administration, ocular administration, and topical administration, and nanoparticles for protein peptide delivery. Nano carrier systems can also be subcategorized based on the degree of their degradability (6).

3. Characterization of SLNs: (26)

3.1. Measurement of particle size and zeta potential

Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for routine measurements of particle size PCS (also known as dynamic light scattering) measures the fluctuation of the intensity of the scattered light which is caused by particle movement. This method. Covers a size range from a few nanometers to about 3 microns. PCS is a good tool to characterize nanoparticles, but it is not able to detect larger micro particles Electron Microscopy provides in contrast to PCS and LD, direct information on the particle shape. The physical stability of optimized SLN dispersed is generally more than 12 months. ZP measurements allow predictions about the storage of colloidal dispersion (2) (8).

3.2. Scanning electron microscopy (SEM)

Examination with direct visualization. Techniques based on electron microscopy offer several benefits in morphological analysis; however, they provide limited information on the size distribution. The mean size obtained Scanning electron microscopy (SEM) provides a morphological by SEM is comparable with the results obtained by dynamic light scattering. In addition, these techniques are time-consuming, expensive, and on size distribution (5).

3.3. Transmission electron microscope

The preparation of the sample for the transmission electron microscope is complex and time consuming. They are fixed using a negative staining material, such a uranyl acetate, etc., the characteristics of the sample surface are obtained when an electron beams transmitted through an ultra-fine sample (5).

3.4. Surface hydrophobicity

The hydrophobicity of the surface can be determined by various techniques, such as hydrophobic interaction chromatography, biphasic partition, etc. X-ray photon correlation spectroscopy allows the identification of specific chemical groups on the surface of SLNs (5).

3.5. Dynamic light scattering (DLS)

Currently, the fastest and most popular method for particle size determination by photon correlation spectroscopy (PCS) or dynamic light distribution (DLS). DLS is widely used to determine the size of Brownian nanoparticles in colloidal suspensions in Nano and submicron environments (5).

3.6. Powder X-ray diffraction and differential scanning calorimeter (DSC)

The geometric scattering of radiation from crystal planes within a solid allow the presence or absence of the former to be determined thus 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 (2).

4. Route of administration proposed for SLNs

The most commonly proposed administration route for lipid-based nanosystems is the parenteral route, closely followed by the oral route. Both administration routes seek to achieve systemic effects of the encapsulated drugs, but the trend described is opposite to the current distribution of pharmaceutical products in the market. Where the oral route of administration is the preferred and most widely used route for drug administration.

Parenteral routes, on the other hand, all one the delivery of drugs directly to the systemic circulation with no absorptive barriers to overcome or with minimal restrictions, as in the case of the intramuscular and/or subcutaneous route. More than 50% of the lipid Nano systems assayed by parenteral routes (46 out of 81) corresponds to anticancer drugs, a therapeutic field where IV route remains predominant, in spite of its non-negligible negative aspects, such as invasiveness, associated risks, inability to self-manage and higher technological (7) (9).

5. Applications of SLNs

5.1. SLNs for Parenteral Application: (10) (11)

SLN are very suitable for systemic delivery because they consist of physiologically well-tolerated ingredients and they have good storage capabilities after lyophilization and/or sterilization. When injected intravenously, SLN are sufficiently small to circulate in the micro vascular system and prevent macrophage uptake in case of hydrophilic coating. Therefore, SLN have been suggested for viral and non-viral gene delivery. Cationic SLN has been demonstrated to bind genes directly via electrostatic interactions, and have potential benefits in targeted gene therapy in treatment of cancer.

5.2. SLNs for nasal application: (12) (13) (14)

Approaches including formulation development and prodrug derivatization have been used to increase drug absorption through the nasal mucosa. SLN has been approached by many research groups as an alternate Trans mucosal delivery route for macromolecular therapeutics and diagnostics. Coating polymeric nanoparticles with PEG yielded promising results as vaccine carriers, according to a recent study.

Tobio concluded effectiveness with PEG coating of polylactic acid nanoparticles in increasing transmucosal transport of the encapsulated bioactive chemical. This idea could be used to solid lipid nanoparticles.

They discovered that a lipid matrix that is solid at body temperature is ineffective for diazepam rectal administration. In their next trials, they decided to use lipids that melt at body temperature. This region appears to be ideal for research, especially when the benefits of the rectal route are considered. PEC coating appears to be a potential method for rectal distribution and, as a result, enhanced bioavailability.

5.3. SLNs for respiratory application: (15) (16) (24)

Application of Respiratory system by minimizing first-pass effects, the lungs provide a large surface area for drug absorption due to SLNs. Because the walls of alveoli in the deep lung are extremely thin, rapid drug absorption by inhalation of medicines (in the 1-3 um. size range) occurs .In the uptake of nanoparticle in the respiratory system, lymphatic drainage plays a vital function. SLNs could be used as carriers for anti-cancer medicines or peptide therapies to increase their bioavailability in lung cancer treatment. The bio distribution of inhaled radio-labeled SLNs were examined, and the results revealed a considerable absorption of radio-labeled SLN into the lymphatic after inhalation.

5.4. SLNs for Ocular Application: (17) (18)

SLNs administration of ocular drugs has been described numerous times with the aim of ocular drug targeting, SLN's biocompatibility and mucoadhesive qualities enhance its interaction with the ocular mucosa and prolong the drug's corneal contact time. Cavalli et al was investigated the use of SLN as tobramycin carriers in rabbit eyes. As a result, SLNs enhanced medication bioavailability in the vitreous significantly. Cavalli was looked into the delivery of pilocarpine by SLN, which is routinely used in glaucoma treatment. They observed remarkably similar findings in order to improve drug absorption in the eyes.

5.5. SLN for Rectal Application: (19)

In the literature, there are a few reports on rectal drug administration using SLN .In order to offer rapid effect diazepam with SLN for rectal delivery. They gave SLN dispersions to rabbits and tested their bioavailability.

They discovered that a lipid matrix that is solid at body temperature is not an advantageous approach for diazepam rectal distribution in their next trials, they opted to use lipids that melt at body temperature. This region appears to be ripe for research, especially when the advantages of the rectal route are considered. PEG coating appears to be a promising method for rectal administration and, as a result, increased bioavailability was seen.

5.6. SLN for Topical application: (20)

SLNs 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. They are well suited for use on damaged or inflamed skin because they are based on non-irritant and non-toxic lipids that shows SLN as a good formulation for topical application.

5.7. SLN in Cancer chemotherapy: (21) (22)

Several chemotherapeutic agents have been encapsulated in SLN and their in vitro and in vivo efficacy has been studied during the last two decades. Tamoxifen, an anticancer medicine, has been included into SLN to prolong the drug's release after I.V. Administration in breast cancer patients. SLN with medicines like methotrexate and camptothecin has been used to target tumors. Metoxantrone SLN local injections were developed to lower toxicity while also improving the drug's safety and efficacy in the treatment of breast cancer and lymph node metastasis.

5.8. SLN for potential agriculture application: (23) (25)

Essential oil extracted from Artemisia arborescence L. when incorporated in SLN, were able to reduce the rapid evaporation compared with emulsions and the systems have been used in agriculture as a suitable carrier of ecologically safe pesticide.

6. Conclusion

The Solid lipid nanoparticles are very essential to get greater bioavailability .BCS class ll and class lV drugs are less soluble, so shows less pharmacological action because of less permeability, by adding lipid we can increase the drug solubility .And also decreasing particle size we can enhance the dissolution and rate of absorption, so we get more pharmacological action due to more bioavailability. Solid lipid nanoparticles are innovative drug delivery system to improve bioavailability of drugs and pharmacological action.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

References

[1] Müller, Rainer H.; Mäder, Karsten; Gohla, Sven (3 July 2000). "Solid lipid nanoparticles (SLN) for controlled drug delivery – a review of the state of the art". European Journal of Pharmaceutics and Biopharmaceutics. 50 (1): 161–177. doi:10.1016/S0939-6411(00)00087-4. PMID 10840199

[2] Solid Lipid Nanoparticles: A Review P. Ekambaram, A. Abdul Hasan Sathali* And K. Priyanka Department of Pharmaceutics, College of Pharmacy, Madurai Medical College, MADURAI – 625020 (T.N.) INDIA (Received: 10.10.2011; Revised: 22.10.2011; Accepted: 25.10.2011)

[3] Attama AA. SLN, NLC, LDC: state of the art in drug and active delivery. RecentPat Drug Deliv Formul. 2011 Sep;5(3):178-87. doi: 10.2174/187221111797200524. PMID: 21834777.

[4] Jenning V, Thünemann AF, Gohla SH. Characterisation of a novel solid lipid nanoparticle carrier system based on binary mixtures of liquid and solid lipids. Int J Pharm. 2000 Apr 20;199(2):167-77. doi: 10.1016/s0378-5173(00)00378-1. PMID: 10802410.

[5] Safiya Shaikh, Himanshu Verma, Nirmal Yadav, Mirinda Jauhari, Jyothi Bullangowda, "Applications of Steroid in Clinical Practice: A Review", International Scholarly Research Notices, vol. 2012, Article ID 985495, 11 pages, 2012. https://doi.org/10.5402/2012/985495.

[6] Duan, Yongtao; Dhar, Abhishek; Patel, Chetan; Khimani, Mehul; Neogi, Swarnali; Sharma, Prolay; Siva Kumar, Nadavala; Vekariya, Rohit L. (2020). A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems. RSC Advances, 10(45), 26777–26791. doi:10.1039/d0ra03491f .

[7] Scioli Montoto, SebastiÃ¡n; Muraca, Giuliana; Ruiz, MarÃa Esperanza (2020). Solid Lipid Nanoparticles for Drug Delivery: Pharmacological and Biopharmaceutical Aspects. Frontiers in Molecular Biosciences, 7(), 587997–. doi:10.3389/fmolb.2020.587997.

[8] Garud, Akanksha; Singh, Deepti; Garud, Navneet (2012). Solid Lipid Nanoparticles (SLN): Method, Characterization and Applications. International Current Pharmaceutical Journal, 1(11), – . doi:10.3329/icpj.v1i11.12065.

[9] K. Westesen and B. Siekmann. Biodegradable colloidal drug carrier systems based on solid lipids. In S. Benita (ed.), Microencapsulation, Marcel Dekker, New York, 1996 pp. 213-258.

[10] Wissing SA, Kayser O, Müller RH. Solid lipid nanoparticles for parenteral drug delivery. Adv Drug Deliv Rev. 2004 May 7;56(9):1257-72. doi: 10.1016/j.addr.2003.12.002. PMID: 15109768.

[11] Vallier L, Reynolds D, Pedersen RA. Nodal inhibits differentiation of human embryonic stem cells along the neuroectodermal default pathway. Dev Biol. 2004 Nov 15;275(2):403-21. doi: 10.1016/j.ydbio.2004.08.031. PMID: 15501227.

[12] Lee A, et al. (1994) Site-directed mutagenesis of the yeast PRP20/SRM1 gene reveals distinct activity domains in the protein product. Mol Gen Genet 245(1):32-44.

[13] Uner, M., & Yener, G. (2007). Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives. International journal of nanomedicine, 2(3), 289–300.

[14] González-Pérez, J. A., González-Vila, F. J., Almendros, G., & Knicker, H. (2004). The effect of fire on soil organic matter—a review. Environment international, 30(6), 855-870.

[15] Garud, A., Singh, D., & Garud, N. (2012). Solid lipid nanoparticles (SLN): method, characterization and applications. International Current Pharmaceutical Journal, 1(11), 384-393.

[16] Videira, M. A., Botelho, M. F., Santos, A. C., Gouveia, L. F., Pedroso de Lima, J. J., & Almeida, A. J. (2002). Lymphatic uptake of pulmonary delivered radiolabelled solid lipid nanoparticles. Journal of drug targeting, 10(8), 607-613.

[17] Friedrich, K., Zhang, Z., & Schlarb, A. K. (2005). Effects of various fillers on the sliding wear of polymer composites. Composites science and technology, 65(15-16), 2329-2343.

[18] Cavalli, R., Gasco, M. R., Chetoni, P., Burgalassi, S., & Saettone, M. F. (2002). Solid lipid nanoparticles (SLN) as ocular delivery system for tobramycin. International journal of pharmaceutics, 238(1-2), 241-245.

[19] Sznitowska, M., Zurowska-Pryczkowska, K., Dabrowska, E., & Janicki, S. (2000). Increased partitioning of pilocarpine to the oily phase of submicron emulsion does not result in improved ocular bioavailability. International journal of pharmaceutics, 202(1-2), 161-164.

[20] Wissing, S. A., & Müller, R. H. (2003). Cosmetic applications for solid lipid nanoparticles (SLN). International journal of pharmaceutics, 254(1), 65-68.

[21] Murthy, M., Ranjan, R., Denef, N., Higashi, M.E., Schupbach, T., Schwarz, T.L. (2005). Sec6 mutations and the Drosophila exocyst complex. J. Cell Sci. 118(Pt 6): 1139--1150.

[22] Journal of Pharmacology 22. Wong, H. L., Bendayan, R., Rauth, A. M., Xue, H. Y., Babakhanian, K., & Wu, X. Y. (2006). A mechanistic study of enhanced doxorubicin uptake and retention in multidrug resistant breast cancer cells using a polymer-lipid hybrid nanoparticle system and Experimental Therapeutics, 317(3), 1372-1381.

[23] Casagrande R, Georgetti SR, Verri WA Jr, Jabor JR, Santos AC, Fonseca MJ. Evaluation of functional stability of quercetin as a raw material and in different topical formulations by its antilipoperoxidative activity. AAPS PharmSciTech. 2006 Feb 3;7(1):E10. doi: 10.1208/pt070110. PMID: 16584140; PMCID: PMC2750709.

[24] Bhalekar, M., Upadhaya, P. & Madgulkar, A. Formulation and characterization of solid lipid nanoparticles for an anti-retroviral drug darunavir. Appl Nanosci 7, 47–57 (2017). https://doi.org/10.1007/s13204-017-0547-1

[25] Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: a modern formulation approach in drug delivery system. Indian J Pharm Sci. 2009 Jul;71(4):349-58. doi: 10.4103/0250-474X.57282. PMID: 20502539; PMCID: PMC2865805.

[26] Anand Kumar Kushwaha, Parameswara Rao Vuddanda, Priyanka Karunanidhi, Sanjay Kumar Singh, Sanjay Ekambaram P, Abdul HS. Formulation and evaluation of solid lipid nanoparticles of ramipril. J Young Pharm. 2011 Jul;3(3):216-20. doi: 10.4103/0975-1483.83765. PMID: 21897661; PMCID: PMC3159275.