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A COMPREHENSIVE LITERATURE REVIEW ON SOLID LIPID NANOPARTICLES

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ABSTRACT

Solid lipid nanoparticles (SLNs) are nanoscopic (50–1000 nm) colloidal carriers consisting of solid lipids. The internal core structure of SLNs is easily adaptable to lipophilic compounds. One of the potential pharmaceutical nano carriers developed for regulated drug delivery are solid lipid nanoparticles (SLNs), also known as lipospheres. Solid lipids, especially physiological lipids, that have been successfully dispersed in an aqueous solution along with a stabilising agent (surfactant) and co-surfactants that may ensure particular qualities are the active major constituents of SLNs. These substances can be synthesised in large amounts, regularly biodegrade, and exhibit high levels of stability. These SLNs are created with biodegradable components. They should be non-toxic or low in toxicity, have a high surface area, and release drugs gradually with the fewest probable side effects. In recent years, the pharmaceutical and medical industries have seen a growth in the use of SLN drug delivery,

ultrasonic drug and gene delivery, cancer chemotherapy, targeted brain drugs delivery, delivering peptides and proteins, and cosmetic and dermatological preparations. The characteristics of SLN include high stability, decreased toxicity, better bioavailability of bioactive substances that are weakly water soluble, and protection of pharmaceuticals that are entrapped from sensitive environments. Solvent-based, non-solvent, and other preparation methods are used to create the SLN. SLNs have been created for a variety of uses, including pharmacological, biological, cosmetic, and nutraceutical ones. Solid lipid nanoparticles (SLNs), which are nontoxic, biocompatible, and simple to make, could be able to help.

Keywords: Solid lipid nanoparticles, drug delivery, nonsolvent method

INTRODUCTION

The 1991 introduction of solid lipid nanoparticles (SLN) as a substitute for conventional colloidal carriers such emulsions, liposomes, and polymeric micro- and nanoparticles **[1]**. One of the promising pharmaceutical nanocarriers designed for regulated drug delivery is solid lipid nanoparticles (SLNs), originally known as lipospheres **[2]**. Solid lipid nanoparticles (SLNs) are colloidal carriers of nanoscopic size (50–1000 nm) composed of solid lipids **[3, 4]**. Lipophilic compounds can easily fit in the SLNs' internal core structure. Solid lipids (mostly physiological lipids) that have been properly dispersed in an aqueous solution with a stabiliser (surfactant) and co-surfactants that may ensure particular qualities are the active key components of SLNs. These substances often allow for large-scale synthesis, have high levels of stability, and are biodegradable. Since the majority of these SLNs are made from biodegradable materials, it is expected that they will have minimal toxicity or won't be harmful, have a high surface area, and release drugs slowly while minimising any side effects **[1, 2, 4, 5]**. Submicron colloidal carriers (SLNs) have thus been proposed to provide combinatorial benefits of polymeric nanoparticulate systems, fat emulsions, and liposomes while avoiding some of these carriers' drawbacks. From the perspective of formulation, SLNs provide superior physical stability, environment protection for labile medicines, and targeted drug administration **[2, 6]**. However, some of the disadvantages of SLNs include inadequate drug loading, drug expulsion, particularly due to phase transition during storage, and relatively high water content. Nanostructured lipid carriers (NLCs), a modified form of SLNs, are being used to lessen these issues **[2]**. While NLC is frequently regarded as the second generation of SLN, SLN was initially reported as the first generation of solid lipid carrier systems in the nanometer dimension **[7]**.

This article aims to provide a quick overview of the various lipid-based carrier systems, including their structure, stability, production methods in use, drug incorporation, and drug release mechanisms.

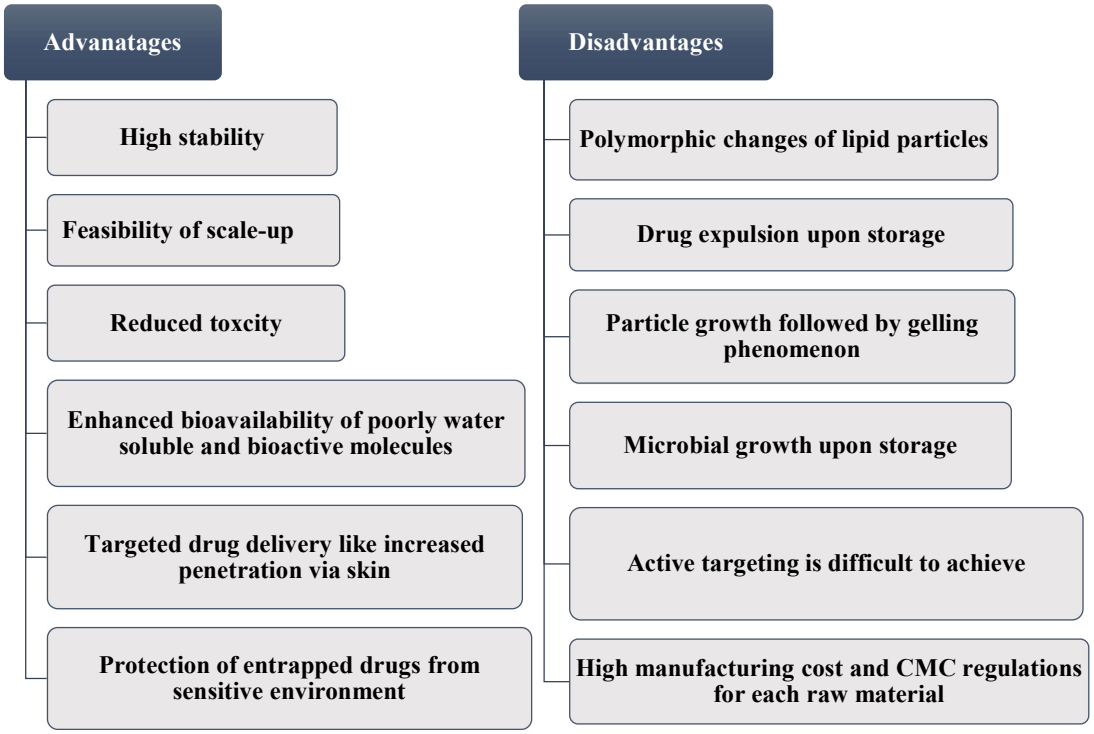

Figure 1: Advantages & disadvantages of SLNs

Figure 2: Applications of SLNs

1. SLNs as therapeutic delivery systems: **[8]**

SLNs have been created for a variety of uses, including nutraceutical, cosmetic, pharmacological, and biological ones. Solid

lipid nanoparticles (SLNs) might be able to help since they are nontoxic, biocompatible, and simple to make. This makes them a promising platform for attaining potential targeted and controlled administration of different therapeutic drugs. By changing the lipid components, the release of drugs from SLNs can be managed **[9]**. SLN formulations have been created and comprehensively described in vitro and in vivo for a variety of administration routes, including parenteral, oral, cutaneous, ophthalmic, pulmonar, and rectal. Recently, a first product—Nanobase by Yamanouchi—which is a topical moisturizer—was released on the Polish market. By changing the lipid components, the release of drugs from SLNs can be managed.

Methods of preparation of SLNs:

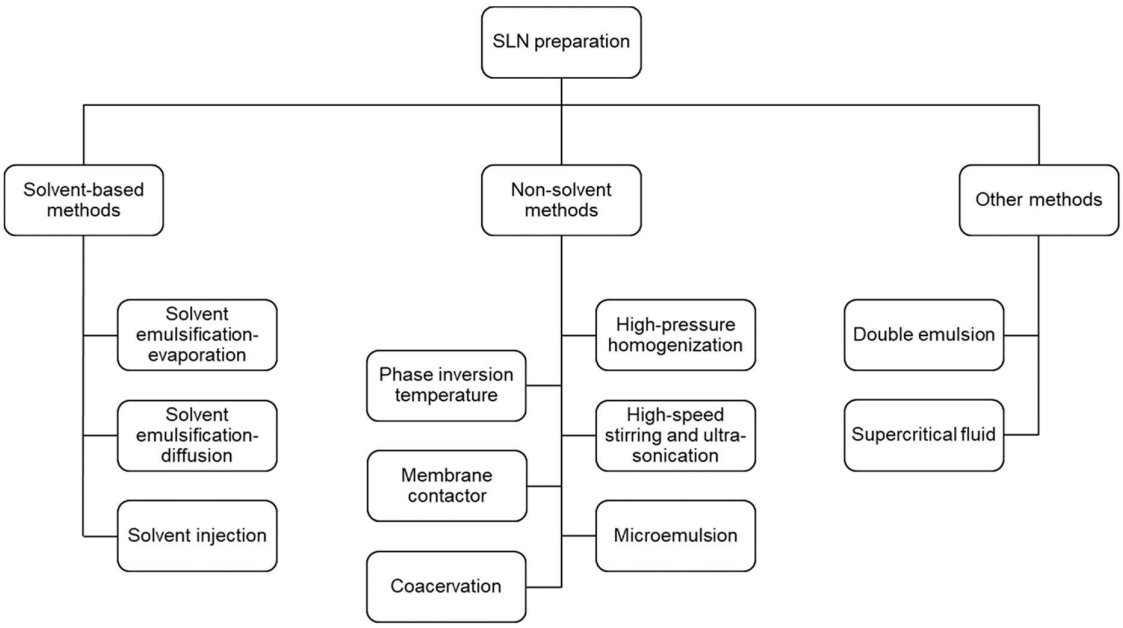

Figure 3: Different method of preparation of SLNs

2. Solvent-Based Methods:

2.1Solvent Emulsification-Evaporation Method: Due to their outstanding biocompatibility, high drug loading, long-term stability, and viability for large-scale production, solid lipid nanoparticles (SLN), or lipid nanoparticles with solid matrix, are the most intriguing carrier for oral drug delivery. Solid lipid nanoparticles (SLN) were created in this study using a single emulsification-solvent evaporation technique **[8-12]**.

In this procedure, water-immiscible organic solvents including cyclohexane, toluene, and chloroform are used to dissolve the hydrophobic drugs and lipophilic material. The mixture is now emulsified in an aqueous phase using high-speed homogenization. Instantaneously allowing the coarse emulsion to pass through a microfluidizer.

The organic solvent is evaporated in a rotary evaporator under reduced pressure and mechanical agitation at room temperature. Bypassing the heat stress is the major area of this technique's mastery. Therefore, the inclusion of extremely thermolabile drugs is now a possibility.

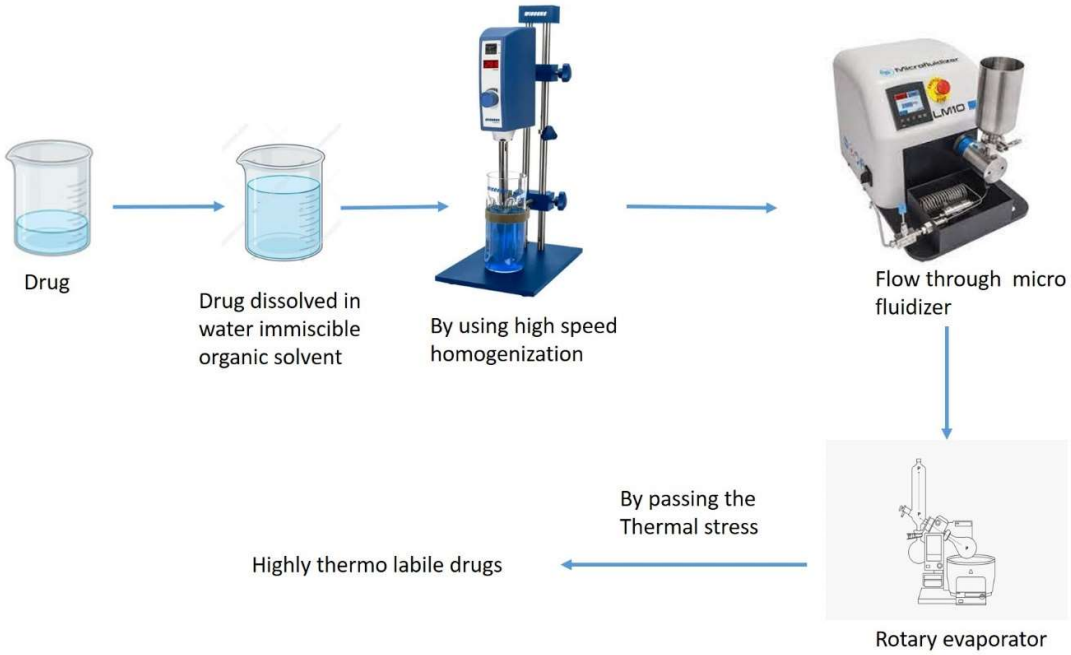

Figure 4: Solvent emulsification evaporation

2.2 Solvent emulsification diffusion: The solvent emulsification-diffusion method was primarily utilised to create polymeric nanocarriers, but it has also been employed to create solid lipid nanoparticles. The solvent emulsification diffusion technology ensures the loading of both hydrophilic and lipophilic drugs, is physically less demanding, and is easily scaleable. The solvent emulsification-diffusion method for creating SLNs entails creating a solvent-in-water emulsion using a solvent that is "partially" water-miscible and contains the lipid in sensible proportions. When the transitory oil-in-water emulsion is poured into water, the lipophilic substance that has been dissolved in the organic solvent instantly solidifies as a result of the organic solvent diffusing from the droplets to the continuous phase **[13-17]**.

2.3 Solvent-injection method: In the solvent injection (or solvent displacement) method, the drug and lipid are dissolved in a water-miscible organic solvent (ethanol, acetone, or isopropanol) and then injected through a syringe needle into water while it is being stirred. The lipid precipitates as nanoparticles when it comes into contact with the water, encasing the drug **[18-21]**.

2.4 Non-solvent methods:

2.4.1 High pressure homogenization: Lipid nanoparticle synthesis using HPH technology has become a well-established and effective process. This method for the mass manufacture of LNs is comparable to previous ways but also applicable. The homogenization process was divided into two distinct phases: hot and cool. In both methods, the drug substance is dissolved or disseminated in the melted lipid prior to the HPH. Fluid is moved in the homogenizer's small gap by high pressure (100–2000 bar). Sub-micron is the range for the average particle size. Homogenization has a number of benefits, such as mass production, the absence of organic solvents, enhanced product stability, and improved drug loading, but its use is problematic due to special high pressure and temperature conditions **[22, 23]**.

2.4.2 Hot homogenization: This method, which chooses temperatures over the lipid's melting point, is thereafter referred to as homogenising an emulsion. For the lipid and drug combination at the same temperature, an aqueous surfactant is used. A hot pre-emulsion is prepared using a high shear mixing apparatus, creating an emulsion of the oil in water type. The product is then allowed to cool, which starts the development of lipid crystals and SLNs later on. Three to five rounds of homogenization at a pressure of 500 to 1,500 bar are required to produce excellent SLNs. It is important to always be aware that HPH causes a rise in temperature. The number of cycles or pressure increase causes a growth in the particle size. The forces of attraction between the particles, which result from the energy of the particles' motion, are to blame for this. The nano emulsion is then cooled to room temperature, when the recrystallization of lipids takes place and nanoparticles are produced **[24]**.

2.4.3 Cold homogenization: The development of cold homogenization addresses a number of issues with hot homogenization, including temperature-induced drug degradation, drug distribution into the aqueous phase during homogenization, and complexity of the nano emulsion's crystallisation step, which can result in multiple modifications and/or super cooled melts. In this method, the drug-containing lipid melt is cooled before being crushed into tiny particles and dispersed in a cold surfactant solution to create a pre-suspension. Following homogenization of the pre-suspension at or below room temperature, the gravitational pull of the solid lipid nanoparticles is strong enough to shatter the lipid microparticles into smaller pieces **[25, 26]**.

2.4.4 Phase-Inversion temperature: The phase-inversion temperature method (PIT) is a low-energy technique that relies on variations in the solubility of polyethoxylated non-ionic surfactants as a

function of temperature. High temperatures cause the surfactant to transition from being hydrophilic to hydrophobic, which results in negative curvatures and reverse micelles that are bloated with water. There is zero spontaneous curvature and very low interfacial tension values when the surfactant has an affinity for both the water and oil phases at a certain temperature. Hydrated non-ionic surfactants have a high-water solubility when the temperature falls below TPIT and often form tiny droplets. For making nano emulsions that contain a volatile oil, the PIT approach has been employed frequently **[27, 28]**.

2.4.5 Membrane Contactor: This process involves pressing a lipid through a membrane contactor at a temperature over its melting point. Water circulating beyond the pores flows with the formed droplets of melted lipid, which is then further cooled at room temperature **[29, 30]**. On the lipid phase flow and the SLN size, the effects of the formulations for the aqueous phase and lipid phase are investigated **[31]**.

2.4.6 Coacervation: The production of SLN **[32]** using this straightforward, solvent-free process relies on heating water solutions containing a particular salt of fatty acids over their Krafft threshold. One of the key components of this approach is heating the lipid's solution, as the Krafft Point is the temperature at which a surfactant's solubility equals the critical micellar concentration. The stabiliser solution and a coacervating agent are added after that to generate the emulsion and to cause the pH to shift, which will cause SLN to develop. Then, this mixture is swiftly chilled while continually being stirred. Three major hypotheses—a drug-enriched core, a drug-enriched shell, and a homogeneous matrix—have been shown to be viable options for drug distribution within solid lipid nanoparticles **[33-36]**.

2.4.7 High-speed stirring and ultra-sonication: Ultrasonication and high-speed stirring (high-shear homogenization) are common dispersion methods. One of the easiest and most affordable methods for creating SLNs is high-speed stirring. This technique involves melting lipids at high temperatures (5–10 °C above the melting point of solid lipids) before dissolving or dispersing medicines uniformly inside the molten lipids. The drug-lipid melt is then combined with an aqueous phase containing surfactants (also at the same temperature), and the mixture is homogeneously dispersed using a high-shear mixer. Due to the shear of extremely turbulent eddies, a hot oil/water (o/w) emulsion is created. By cooling these dispersions, SLNs are created. Ultrasonication, which separates droplets based on the creation, expansion, and implosive collapse of bubbles, is typically performed after this high-speed stirring. Because sonication energy is not distributed

equally throughout the batch when ultrasonication is done without the high-shear mixing stage, SLNs and NLCs generated have a wide spread. To produce SLNs dispersions with narrow particle distributions, high-speed stirring and ultrasonication have frequently been combined **[37-40]**.

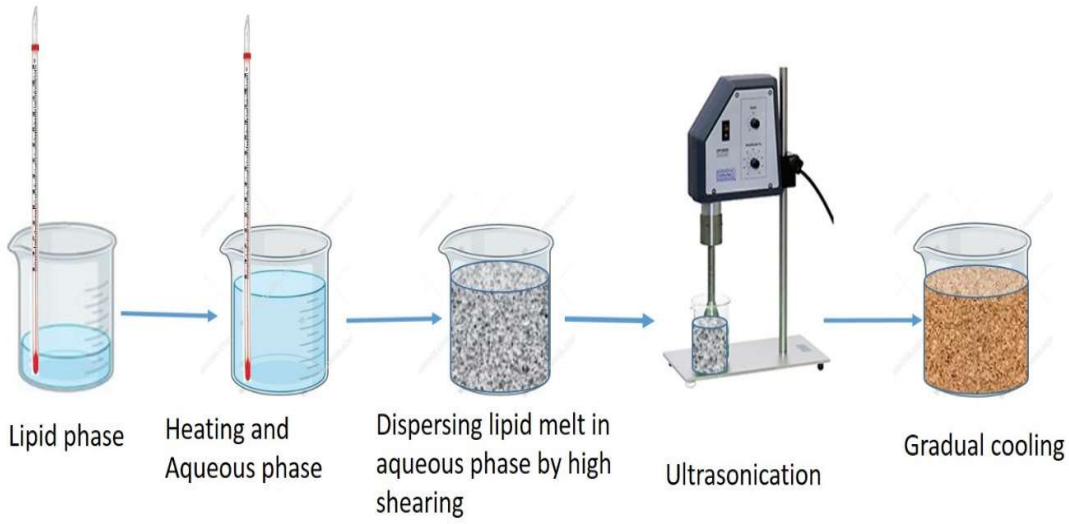

Figure 5: Ultra sonication

2.4.8 Micro emulsion: SLN preparation using a microemulsion template. To create a transparent O/W microemulsion while stirring, her innovation calls for heating lipids over their melting point and adding an aqueous phase containing surfactants and co-surfactants at the same temperature. You can prepare more than one W/O/W. Prior to diluting the aforementioned microemulsion in cool water (2–10°C), drugs and active ingredients can be added to it to produce solid lipid nanoparticles with a narrow size distribution and smaller mean particle size. Triglycerides, fatty acids, or fatty alcohols can all be used as lipids in this process. Bile salts, phospholipids, polysorbates, short-chain fatty acids (butyric acid, hexanoic acid), phosphoric acid alkyl esters, and benzyl alcohol are all options for surfactants. Short-chain alcohols and glycols (buthanol, hexanol, hexanediol, and propylene glycol) are other options. A amount of water 10 to 200 times as large as the microemulsion's volume can be used to dilute it. Surfactants and cosurfactants may be partially removed from a suspension of nanoparticles by diafiltration **[41-43]**.

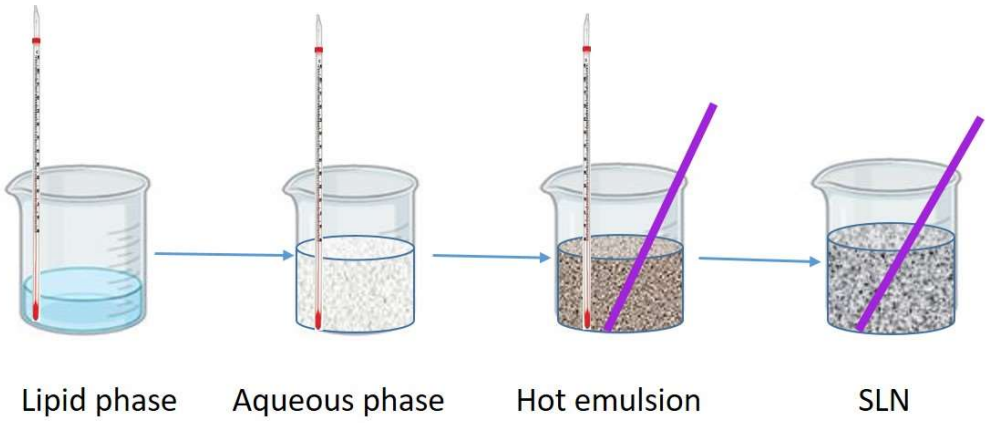

Figure 6: Micro emulsion

2.5 Other methods:

2.5.1 Double Emulsion: SLNs were created using a method that uses no organic solvent and combines the ideas of melt dispersion and double emulsion to create solid lipid particles as small as possible **[44]**. To avoid drug partitioning to the exterior water phase of the w/o/w double emulsion during solvent evaporation, the hydrophilic drug is here encapsulated with a stabiliser **[45]**.

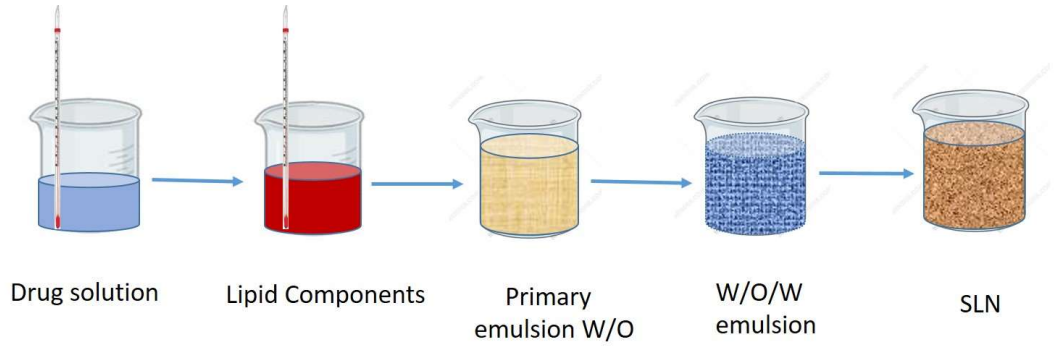

Figure 7: Double emulsion

2.5.2 Supercritical fluid extraction of emulsions: A SCF is any substance that shows both gaseous and liquidus qualities when it is heated or compressed over its critical point. High diffusivity and low viscosity characterise SCFs **[51]**. The production of micro/nanoparticles with a narrow size distribution, better flowability, less residual organic solvent, and high encapsulation efficiency for various types of drugs has been proposed as a benefit of supercritical fluid (SCF), which is based on the solvent extraction of oil-in-water (o/w) emulsions using supercritical carbon dioxide (CO2). The process is touted as being ecologically benign and having the ability to be scaled up, and the final product is said to be a dry powder that makes it easier

to produce better liquid or solid drugs formulations **[46-50]**. SCFs have been employed in place of toxic organic solvents in a number of medicinal applications, including extraction and particle formation procedures. It has been frequently used in the pharmaceutical industry to create supercritical antisolvents (SAS) and rapid expansion supercritical solutions (RESS), both of which use SCF as a solvent **[51]**.

2.6 Research works progress on SLNs:

1. 5-Fluorouracil (5-FU) is a commonly used treatment for colorectal cancer (CRC), but due to its fast metabolism and systemic instability (short half-life), it has not been as effective as it may be.A high payload of 5-FU can be delivered by solid lipid nanoparticles (SLN) to treat CRC
2. Emodin (EMO)-loaded solid lipid nanoparticles (E-SLNs) and assess their in vitro anticancer efficacy. By means of high pressure homogenization (HPH), E-SLNs were created using EMO and pharmaceutical lipid material. The surfactants employed were Poloxamer 188 and Tween 80. E-SLNs were a promising vehicle for oral drug delivery since their drug release may last for up to 72 hours and had a sustained profile. E-SLNs increased the rate of apoptosis in MCF-7 cells, suggesting that cell cycle arrest and apoptosis may be the underlying mechanism of the enhanced cytotoxicity. All things considered, it appears that HPH was a quick, accessible, and efficient way to create high-quality E-SLNs and increase their water solubility. Additionally, these findings imply that delivering EMO in the form of lipid nanoparticles may be a promising strategy for the treatment of cancer.
3. Aloe-emodin (AE), which has strong action against a variety of tumours including breast cancer, liver cancer, and lung cancer, is a promising anti-tumor candidate. because of its weak solubility in water and low absorption, AE has a limited clinical application.AE-SLNs), which are solid lipid nanoparticles that have been loaded with AE in an effort to increase the anti-cancer effectiveness of AE. Using the high pressure homogenization (HPH) process, AE-SLNs were created with an optimised prescription. The AE-SLNs ultimately demonstrated stable particle size at 88.9 5.2 nm, optimal drug entrapment efficiency (EE) of 97.71 0.5%, and good stability with regard to zeta-potential as high as -42.8 mV. AE was able to achieve

sustained release by loading into SLNs, according to the in vitro release profiles. Based on these results, we think that creating AE-SLNs is a good strategy to increase the anti-cancer effectiveness of AE.

4. The goal of the current work was to create solid lipid nanoparticles (SLNs) that contained curcumin by combining liquid and solid lipids. This improved curcumin's chemical stability and dispersibility, prolonged its antitumor action, increased cellular absorption, and increased bioavailability. Through the use of liquid lipid Sefsol-218(®), curcumin-loaded SLNs (C-SLNs) were created. Investigated were curcumin's shape, stability, and release in the improved formulation. Curcumin showed an enhanced chemical stability two-phase sustained release profile from C-SLNs C-SLNs demonstrated sustained inhibitory efficacy in cancer cells in comparison to the solubilized solution, as well as time-dependent increases in intracellular absorption. The bioavailability of curcumin was raised 1.25-fold in rats after intravenous treatment. Successful development has been made of C-SLNs with enhanced chemical stability and dispersibility in aqueous systems. A useful method of delivering curcumin for the treatment of cancer may be C-SLNs.
5. A growing body of research suggests that andrographolide (ADG) has anti-cancer properties against several cancer cell lines. Find out if the presence of ADG-SLN improved the bioavailability and anti-cancer effectiveness of ADG in human immortalised oral epithelial (HIOEC), precancerous leukoplakia (Leuk1), HN6, and HN30 cells, which served as an in vitro model of stepwise head and neck squamous cell carcinoma progression. However, its limited clinical use as a chemo preventative drug is due to its high hydrophobicity and low absorption. ADG-SLN promoted cell cycle arrest and apoptosis more potently than free ADG. When compared to free ADG, ADG-SLN had stronger inhibitory effects on head and neck cancer and precancerous cells. This result is brought about by ADG-SLN's more effective cellular uptake and intracellular absorption.
6. Metastasis is the main reason why women die from breast cancer solid lipid nanoparticle-docetaxel's (SLN-Docetaxel) anticancer properties The high-energy technique was used to

create solid lipid nanoparticles (SLNs). Pluronic F127 and Span 80 were chosen as the surfactants to stabilise nanoparticle dispersion, and Compritol 888 ATO was chosen as the lipid matrix. For at least 120 days, the particles were highly stable. when applied to the management of metastatic breast tumours in BALB/c mice. Through tumour volume reduction (p 0.0001) and the prevention of spontaneous lung metastasis in 4T1 tumor-bearing mice, in vivo experiments demonstrated that SLN-DTX had greater anticancer activity than free docetaxel. Lung histological investigations verified that SLN-DTX therapy could stop tumour growth. A promising delivery system for the treatment of breast cancer and the prevention of metastases may be DTX-loaded SLNs.

7. Create folic acid-doxorubicin (FAD) conjugate-loaded solid lipid nanoparticles (SLNs) coated in tween 80 for site-specific medication delivery to brain cancer cells. The average particle size of FAD conjugate-loaded SLNs (SLN-C) was determined to be 220.4 2.2 nm, with an entrapment effectiveness of 36.2 0.6%. On U87 MG cell lines, the cytotoxicity and cellular uptake were evaluated. The SLN-C's excellent antitumor activity against brain cancer cells was validated when its half maximal inhibitory concentration value of 2.5 g/ml was discovered.
8. The doxycycline SLNs were lyophilized, and the lyophilization procedure was optimised with cryoprotectant to preserve their physiochemical, antibacterial, and anticancer properties. The SLNs doxycycline dispersion was frozen at -20°C and 10% mannitol was added to create the ideal environment for preventing particle aggregation. There was no burst effect on the doxycycline release profile, according to investigations into the release profile, SEM of lyophilized SLNs, TGA, antibacterial efficacy, and anticancer efficacy. It could be inferred from this that freeze drying doxycycline SLNs improves stability and decreases negative effects.
9. For benign prostate hyperplasia and androgenic alopecia, finasteride is thought to be the best treatment. Create finasteride nanodrug carriers with improved skin retention characteristics. For better retentive characteristics, the finasteride was

created as solid lipid nanoparticles that were coated with varying amounts of chitosan. Stearic acid was employed as a solid lipid while PEG-6000 and Tween-80 were used as surfactants in the "high-speed homogenization technique" to create solid lipid nanoparticles (SLNs). Studies on the in vitro drug release from SLNs revealed that after a 4-hour initial burst release, the medication continued to be released for another 24 hours. SLNs coated with chitosan showed a longer drug release as compared to untreated nanoparticles. The formulation of the SLNs for finasteride was successful, and chitosan decorating improved drug retention in the skin layers. These formulations could be utilised to treat benign prostatic hyperplasia and androgenic alopecia without the negative side effects, medication degradation, or protracted drug use associated with conventional oral therapy.

10. Lovastatin is a hypolipidemic drug used to lower blood cholesterol levels; because of this, it is a good candidate for transdermal delivery. Additionally, lipid nanoparticles, particularly SLNs, are good carriers for the delivery of active ingredients through a variety of routes, including transdermal, nasal, oral, and intravenous. A straightforward, dependable, and adaptable process known as the solvent emulsification diffusion technique was used to create lovastatin-loaded SLN. The SLNs also displayed mixed order kinetics sustained release that lasted up to 24 hours. Therefore, the goal of the current work was to create SLNs that were loaded with lovastatin. These SLNs could then be added to suitable gel or cream for topical administration to the skin, which could be a good substitute for taking lovastatin orally.
11. Create and test a variety of chitosan and poly(2-ethyl-2-oxazoline)-coated solid lipid nanoparticles for ciprofloxacin administration. Combining melt-emulsion sonication and low-temperature solidification techniques, a formulation of poly(2-ethyl-2-oxazoline) (PSLN) containing ciprofloxacin was created. Compared to chitosan-coated solid lipid nanoparticles (CSLN), PSLN had a greater encapsulation effectiveness. All of the formulations showed an early burst release of the medication in vitro, followed by a continuous release over the course of 24 hours.

Comparing CSLN to PSLN, increased flux and apparent permeability were also seen, along with higher mucoadhesion and retention on ocular tissues, but decreased entrapment efficiency.

12. albendazole (ABZ) solid lipid nanoparticles (SLN) and assess its effectiveness in mice model after oral treatment. Compritol 888 ATO was used as the lipid and Cremophor EL and Tween 80 were used as the surfactants to manufacture SLN of ABZ utilising the phase inversion temperature method. The average particle size of ABZ-SLN was determined to be between 116 and 168.3 nanometres, and the entrapment efficiency ranged from 82.99 to 89.72 nanometres, depending on the drug concentration. The simulated gastrointestinal circumstances used in the in vitro drug release profile of ABZ-SLN showed a prolonged release pattern, with the maximal release found to be 92.661.7% in 24 hours. The reduction in larvae count in the liver, lung, brain, and kidney was confirmed by the anthelmintic efficacy investigation. The findings suggest that ABZ solid lipid nanoparticles may represent a potential formulation for the treatment of Toxocaracanis infection.
13. Solid lipid nanoparticles were created utilising a melt-emulsification and ultrasonication technique. They were loaded with sodium aescinate. The negatively charged, spherical, solid lipid nanoparticles with a size of 109.4 nm and an encapsulation effectiveness of up to 86.6% were loaded with sodium aescinate. Both single- and double-emulsified solid lipid nanoparticles showed continuous release for 12 hours without an initial burst release. The outcomes demonstrated that solid lipid nanoparticles loaded with sodium aescinate through twofold emulsification exhibited greater drug loading and stability following reconstitution. In comparison to free sodium aescinate, the sodium aescinate-solid lipid nanoparticles with double emulsification showed higher anti-inflammatory action, including paw and ear swelling in mice. As a result, solid lipid nanoparticles have enormous potential for use as a sodium aescinate delivery system in medical applications.
14. The flavonoid myricetin has anticancer effects. S olid lipid

nanoparticles (SLN), coated with chitosan (CS), and active-targeted with folic acid (FA) are used to mimic myricetin. we prepared myricetin-SLN by homogenising and ultrasonically combining FA-bound CS. Both in vitro and in vivo testing revealed that myricetin-SLN-CS-FA was more hazardous to cancer cells than free myricetin. The expression of antioxidant genes reduced, apoptotic genes were changed, and the intrinsic apoptotic pathway was activated in the treated cells. Myricetin-SLN-CS-FA has been shown to have anti-angiogenesis properties by CAM and molecular analysis, as well as anti-tumor properties in vivo by histological staining and molecular analysis. Our in vitro and in vivo research suggests that myricetin-SLN-CS-FA can successfully treat breast cancer.

15. The anti-metabolite medication methotrexate is preferred. It is used to treat several cancers, including lung, skin, and breast cancer. Create and characterise solid lipid nanoparticles with methotrexate loaded using the microemulsion method. By changing the quantity of the surfactant, solid lipid nanoparticles made of glycerol monostearate and stearic acid are produced. For the synthesis of methotrexate solid lipid nanoparticles, glycerol monostearate was shown to be superior to stearic acid due to its smaller mean particle diameter (238.8 nm), higher stability (-56.5 mV), and higher entrapment effectiveness.
16. Create and assess solid lipid nanoparticles (SLNs) of the anti-HIV medication ritonavir that target intestinal lymphatic capillaries and improve bioavailability when administered orally. SLNs were created by first evaporating the solvent, then using Compritol 888 and sodium lauryl sulphate to ultrasonically dissolve them. The average particle size for the improved formulations was substantially below 300 nm, and acceptable ranges for zeta potential and PDI were also discovered. 53.20 4.13 to 73.04 2.85% was the range of the encapsulation efficiency. Images from scanning electron microscopy showed that the medication had completely dissolved within the lipid structure. The results of the pharmacokinetic studies showed that the spleen and thymus had much higher levels of solid lipid nanoparticle absorption than did the

plasma, suggesting that the formulations could improve bioavailability and intestinal lymphatic target specificity.

17. Cisplatin (Cis diamine dichloro platinum) is a platinum drugs that is frequently used to treat lung, head and neck, ovarian, and testicular cancer. It was the first platinum agent to be utilised as an anticancer drug. Among other colloidal carriers, solid lipid nanoparticles (SLNs) were discovered to be the best vehicle for lipophilic drugs due to their improved stability and release delaying properties. By using the microemulsion process, cisplatin-loaded solid lipid nanoparticles were created. As a lipid, stearic acid was employed. The remaining excipients included DPPG, Soy lecithin, Poloxamer P407, acidic buffer PH4, and DPPG. Probe sonication was also employed for 10 minutes at 79 Amplitude. After 48 hours, the total amount of cisplatin released was 82.62 2.04%.
18. Clozapine-loaded solid lipid nanoparticles for use in the treatment of schizophrenia. Soy lecithin and sodium glycolate were used in the precipitation process to create solid lipid nanoparticles. Formulations for nanoparticles were discovered to be in the form of solid dispersion. The formulation's entrapment effectiveness ranged from 20.0 to 52.30%. The zeta potential was discovered to be between -4.42 mv and -74.6 mv. It was determined from this investigation that the manufactured solid lipid nanoparticles of clozapine released the drug well and efficiently.

2.7 QbD approaches on SLNs: The traditional methods for developing pharmaceuticals, which rely on testing to determine quality, are no longer in use. By regulating raw materials (such as medications and excipients) and manufacturing processes, these strategies ensured the quality of the final product. The specifications set forth by regulatory authorities must be met by finished items, and when they are not, manufacturers must redo the process and pinpoint the problems. As a result, testing procedures for quality are costly and can lead to differences that reduce the safety of the final pharmaceutical products. The quality by design (QbD) methodology was developed to address these issues, enhancing production procedures and guaranteeing the high quality and security of finished goods **[52]**. The quality pioneer Dr. Joseph M. Juran created the idea of quality by design (QbD). The US Food and Drug

Administration (FDA) promotes the use of risk-based strategies and QbD principles in the development, production, and regulation of pharmaceutical products. The FDA first placed a focus on QbD after realising that more testing does not always result in higher product quality. The product must be made with quality in mind. With the publication of ICH Q8 (R2) (Pharmaceutical Development), ICH Q9 (Quality Risk Management), and ICH Q10 (Pharmaceutical Quality System), pharmaceutical QbD has advanced over time **[53-55]**. Regarding factors that affect the physical components of the resulting nano systems, many statistical tests and mathematical models have been used. These include variations in composition and production processes (such as emulsification, sonication, and homogenization pressure cycles). These fundamental variables affect zeta potential, mean size, drug encapsulation effectiveness, nanoparticle/globule polydispersity index, and in vitro drug release **[56]**.

D. Patel *et al*. used a QbD strategy to improve topical arginine solid lipid nanoparticles. SLN formulation were effectively generated with decreased particle size and higher% drug loading with effective skin penetration parameters to accomplish the therapeutic effects of Arginine **[57]**.

The Solid Lipid Nanoparticles of Linagliptin were created by D. Krishna Veni *et al*. using the Quality by Design methodology. Production of solid lipid nanoparticles by solvent injection technique and analysis of the impact of crucial process variables and crucial material characteristics on crucial quality metrics **[58]**.

2.8 CONCLUSION:

Lipid nanoparticles are innovative drug delivery technology which provide a variety of benefits beyond existing colloidal and polymeric nanocarriers. Some of the most beneficial features that these lipid carriers offer are simplicity of scaling, biodegradability, enhancing the bioavailability of poorly soluble drugs employing synthetic or natural lipids, biocompatibility, and the ability to develop controlled release rates. For the formulation, characterization, and therapeutic uses of SLN, various approaches are available. Due to their numerous significant features, SLNs have become recognised as effective drug delivery systems, and they will continue to play a vital role in lipid-based drug delivery in the future.

2.9 Expert opinions:

Solid lipid nanoparticles (SLNs) have attracted the attention of formulation and

biomedical researchers. This novel drug delivery technology is beneficial for the controlled and targeted delivery of drugs, vaccines, cosmetics, and biopharmaceuticals, as demonstrated by the remarkable increase in both published research reports and patents in the area of SLNs. Homogenization, microemulsion, and such types of methods can be used to develop SLNs. However, these methods produce solid lipid nanoparticles in different size ranges and distributions. One needs to apply precaution when choosing procedures, chemicals, lipids, etc., for example, the selection of core materials for sheathing or targeting ligands, which create severe issues that are associated with polymeric nanoparticles or whose ingredients are omitted significantly by the SLNs. Another important point is that the choice of an active ingredient may affect physiological processes such as the processing and uptake of drug release from nanoparticles or active ingredient properties such as shape, solubility, etc. Stabilisation of SLNs needs to be careful for long-term storage as dispersion in aqueous medium.

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