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Review Article

## Recent Advances in Solid Lipid Nanoparticle Preparation: Methods, Ingredients, and Routes of Administration

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### Abstract

**Objective:** To identify the importance of Solid lipid nanoparticles (SLNs), their most recent methods of preparation and the drugs, lipid(s) and surfactant(s) most recently used for carrier development. **Methods:** Original articles were identified through searches of MEDLINE/PubMed for within the last 5 years (2020-February 2025), with the following search terms; solid lipid nanoparticles. The main aim was to find original articles/ research, this led to another search but excluded evaluation. **Study Selection and exclusion criteria:** Articles that discussed active pharmaceutical “drugs” were selected for this study and exclusion criteria of “NOT review NOT MRNA NOT DNA NOT RNA” to narrow down the articles. **Data Synthesis:** More than 500 articles were identified and further reviewed in the literature and were categorized according to the method in which the SLN were prepared; homogenization and/or high-pressure homogenization, ultrasonication, solvent injection and/or solvent evaporation phase inversion, microemulsion/emulsification, nano spray drying and/or others and combination methods. **Conclusion:** As more specific drug targeting and drug delivery systems become more of an interest in the drug development field, solid lipid nanoparticles will be of continuance importance for a strategic role in nanoparticle formulations.

**Keywords:** Solid lipid nanoparticles (SLNs), Homogenization, Ultrasonication, Solvent injection

## Introduction

Solid lipid nanoparticles (SLNs) most recently have been of high interest in the pharmaceutical industrial fields. The original/initial methods of preparation of SLNs have been patented by professor Gasco since 1991[1]. However, more recently these methods have been tweaked and modified accordingly to the needs of each researcher for the development of drug incorporated into the solid lipids of nano size.

SLNs are typically made up of a solid lipid, a surfactant, an active pharmaceutical ingredient and aqueous medium such as water. Some solid lipids commonly used, although there is no specific guideline, include stearic acid, glycerol monostearate, and cetyl alcohol [2–4]. Surfactant choice and concentration is important not only to decrease the particle size to nano range but also to ensure stability of the lipid particles produced and prevent aggregation. Too high surfactant concentration may also lead to micelle formation and depending on type of surfactant chosen may lead to toxicity [5]. Surfactants of many types have been successfully used for the preparation of solid lipid nanoparticles; they vary according to their hydrophilicity-lipophilicity balance (HLB). Although majority of surfactants chosen within

previous research were selected based upon popularity and trial and error method, the most commonly include; polysorbates, lecithin's and sorbitan esters [5–7]. SLNs should not be confused with nano lipid carriers which in addition to the compositions of SLNs also include a liquid lipid such as oleic acid, glyceryl tricaprylate, isopropyl myristate and glyceryl dioleate [8,9].

In this review, we aim to identify the importance of SLNs and their methods of preparation, the recent advances and development of different drugs within the nanosized solid lipid core, and finally the advancement in recent research in the formulation of SLNs and the methods in which they were prepared.

## Advantages of SLNs

Solid lipid nanoparticles, are particles of submicron size below 1000 micrometer. Depending on their route of administration they have found to implicate numerous advantages. The use of SLNs have been widely employed to increase solubility of poorly aqueous soluble drugs.

Majority of drugs are delivered via oral route, as it is the most convenient and less invasive method. Research has shown that drug delivery via solid lipid nanoparticles formulations have led to improve bioavailability, reduce

variation in oral absorption, modulate controlled drug release and have shorter onset of action with longer duration times [10–13] .

Advantages of SLNs formulations via ocular route drug delivery systems have found to improve therapeutic efficiency and increase; ocular permeation, drug pre-corneal retention time, ocular bioavailability and distribution, and drug corneal permeability [14–18]. In addition, SLNs have found to prevent ocular toxicity while maintaining sufficient amount of drug in aqueous humor, vitreous humor and retina [14,19].

Transdermal and topical drug delivery systems have numerous biological barriers which limit the use of therapeutic agents. However, the use of nano lipid carriers such as SLNs have been proven to overcome these biological barriers because their nano size can easily allow permeation through the skin. In addition, to the overall modified and controlled drug release, they

promote skin hydration leading to occlusive effects that also aid in drug permeation through the skin. Moreover, the simple components that can be used to formulate SLNs have deemed to be safe on inflamed skin due to their nonirritant and nontoxic nature [20–22]

Nano particles have played an important role in delivery of biological induced drug therapy such as vaccines. They have been widely sought out due to the ability of ease for scaling up manufacturing process. SLNs for parenteral drug delivery have improved bioavailability and like other routes can modify and control drug release. In addition, they have improved stability and have overall reduced clearance and volume of distribution. Due to their nano size researchers have seen enhanced permeability within tumors with increasing retention times leading to a good and promising approach to anticancer targeting drug delivery systems [23–27].

**Table 1: Summary of advantages of SLN according to the route of administration**

Route of Administration	Advantage(s)	Ref
Oral	Improve bioavailability Decrease variation in absorption Modulate controlled drug release Shorter onset of action and longer duration of action	[10–13]
Ocular	Improve therapeutic efficiency Increase ocular permeation Increase drug precorneal retention time Increase ocular bioavailability and distribution Increase drug corneal permeability Prevent/reduce ocular toxicity Maintain sufficient amount of drug in aqueous humor, vitreous humor and retina	[14–19]
Transdermal	Increase permeation through the skin Safe, nonirritant and nontoxic Modified and controlled drug release	[20–22]
Parenteral	Most widely used for biologic delivery as vaccines Improved bioavailability Increase stability Reduce in clearance and volume of distribution Promising approach for anticancer therapy	[23–26]

### Challenges and disadvantages of SLNs

Although the formulation of drugs via solid lipid nanoparticles have been proven to be advantageous, there are still many challenges the researcher may face during the production, storage and administration

process. Overall similar disadvantages and challenges the researcher may face are that since SLNs are lipid in nature, there is a limited loading capacity for hydrophilic drugs, drug expulsion during storage and instability of the lipid sized particles may lead to aggregation during storage leading to particle size growth [10,28–30].

## Methods

An initial search on MEDLINE/PubMed of solid lipid nano particles within the last five years was conducted in February 2025. This led to 1554 results, in order to narrow the scope of literature available this led to a search of "Solid lipid nanoparticles NOT review NOT MRNA NOT DNA NOT RNA". As a result, 923 articles were available for analysis. The main aim was to find original articles/ research designed to determine the different active ingredients, methods of preparations and lipids and surfactants used. This led to another search but excluded evaluation. Finally, 523 articles were subjected for analysis and were carefully read through to determine researches of interest according to criteria.

## Results and Discussion

Accordingly, literature available on PubMed was screened through and summarized according to the method of preparation, active pharmaceutical ingredient, lipid(s) used and surfactant(s) used. These results were summarized and categorized according to the method of which the solid lipid nanoparticles were prepared.

### Methods of preparation of SLNs

Recent literature and investigations have sought out multiple innovative methods of preparing solid lipid nanoparticles. These include; high pressure homogenization, solvent injection/solvent evaporation, phase inversion, microemulsion, ultrasonication and others.

#### High pressure/shear homogenization

The high-pressure homogenization technique is a highly sought out technique due to its simplicity and lack of organic solvent required during processing. This technique requires the preparation of an emulsion consisting of the solid lipid and drug melted to a temperature above the melting point of the lipid followed by addition to the aqueous phase containing the surfactant heated to the same temperature of the lipid solution. This emulsion is then subjected to a high-speed homogenizer with or without pressure as seen by the formation of SLNs of clotrimazole [31]. The presence of pressure is called the high-pressure homogenization method. In the absence of pressure using homogenizer up to 20,000 RPM is known as high shear homogenization method. The homogenizer usually consists of a rotator of high input energy. The emulsion subjected to high speed allows the reduction of particles to a nano size, this emulsion is then allowed to cool for the crystallization of the solid lipid nanoparticles followed by another round of homogenization. Parameters that affect the formation of solid lipid nanoparticles, not only include the formulation design (types and ratios of surfactant and lipid(s) used), but also the rotation speed of the homogenizer, pressure input, time of homogenization and temperature. The main challenge of high-pressure homogenization is the lack of a high energy input homogenizer in small scale laboratories. In addition, the high energy input always leads to increase of temperature of the formulation, thus during the second round of homogenization it is important to keep the system cool as increase in temperature may lead to the coalescence of the particles leading to an increase in size [32].

**Table 2: Recently developed Solid lipid nano particles using homogenization and/or high-pressure homogenization method.**

Method of preparation	Drug(s)	Lipid(s)	Surfactant (s)	Ref
Homogenization	Gemcitabine And oxaliplatin	Cholesterol Oleic acid	Tween 80 Phosphatidylcholine	[33]
Homogenization	Paroxetine	Glycerol monostearate	Tween 80	[34]
High pressure homogenization	Curcumin	Hydrogenated soybean phospholipids	Poloxamer 188	[35]
High shear homogenization	Combined Rhein and Methotrexate	Glycerol palmitostearate	Poloxamer 188	[36]
High pressure homogenization	Beta carotene	Glycerol stearate Medium chain triglyceride	Tween 80	[37]
High pressure homogenization	Abiraterone acetate	Precirol 5 ATO	Kolliphor 188	[38]
High pressure homogenization	Curcumin	Stearic acid	Poloxamer 188	[39]
High pressure homogenization	Cannabidiol	Compritol 888 ATO	Poloxamer 188	[40]
High pressure homogenization	Beta carotene	Hydrogenated sunflower oil	Soy lecithin	[41]
High pressure homogenization	Irenotecan	Tricaprin	Tween 80	[42]

		Triethanolamine	Span 20	
High shear homogenization	Sulconazole	Glycerol monostearate	Tween 20 Phospholipon 90H	[43]
Homogenization	Fexofenadine	Cetyl palmitate	Tween 20	[44]
Homogenization	Rapamycin	Compritol 888 ATO	Tween 80	[45]
Homogenization	P-methoxycinnamic	Cetyl alcohol	Tween 80	[46]
High pressure homogenization	Apixaban	Glycerol monostearate	Polyethylene glycol 200	[47]
High pressure homogenization	Streptomycin sulphate	Precirol 5 ATO	Tween 80 PEG 600 Phospholipon 90G	[48]
Homogenization	Tetrahydro curcumin	Compritol 888 ATO	Tween 80 Phospholipon 90G	[49]
Homogenization	Revaprazan	Precirol 5 ATO	Tween 80	[50]
Homogenization	Pazopanib	Compritol 888 ATO Precirol ATO 5	Tween 80	[51]
Homogenization	Lawsone	Precirol 5 ATO	Tween 80 Poloxamer 407	[52]
High pressure homogenization	Simvastatin	Precirol ATO 5	Poloxamer 407	[53]
High pressure homogenization	Docetaxel	Compritol 888 ATO	Pluronic F127 Span 80	[54]
High pressure homogenization	Combination of Paclitaxel and Curcumin	Compritol ATO 888 Stearic acid	Tween 80	[55]
Homogenization	Valsartan	Precirol 5 ATO	Gelucire 50/13 Pluronic 188	[56]
High pressure homogenization	Monoterpenes (alpha-pinene, citral geraniol or limonene)	Imwitor 900K	Poloxamer 188	[57]
Homogenization	Vancomycin	Lineolic acid	Tween 80	[58]
High pressure homogenization	S-adenosyl-Lmethionine	Tristearin	Tween 80	[59]
High pressure homogenization	Zataria multiflora	Stearic acid	Span 60 Tween 80	[60]
Homogenization	Combination of Donepezil and rhodamine B	Dynasan 116	Tween 80	[61]
Homogenization	Ferulic acid	Compritol ATO 888	Tween 80	[62]
Homogenization	Simvastatin	Compritol ATO 888 Precirol 5 ATO Geleol	Poloxamer 407 Tween 80	[63]
Homogenization	Fucoxanthin	Coconut oil Glyceryl monostearate	Tween 80 Soy lecithin	[64]

Homogenization	Bedaquiline	Lecithin	Tween 80	[65]
Homogenization	Myricetin	Gelucire	Poloxamer 407	[66]
		Compritol 888 ATO		
High pressure homogenization	Curcumin	Compritol 888 ATO	Tween 80	[67]
		Glyceryl monostearate	Phospholipon 90G	
Homogenization	Melatonin	Compritol ATO 888	Poly vinyl alcohol	[68]

### Ultrasonication

Ultrasonication method involves the use of a probe or bath sonicator which allows the breakdown of the formed particles into smaller nano sizes. This method highly depends upon the time of sonication and temperature applied. In addition, sonication of samples

for long periods of time may lead to overheating, thus intermittent sonication has been employed to overcome this problem [69]. Particles developed using ultrasonication method may not be as small as high-pressure homogenization however, combination use with other methods have found successful preparations of solid lipid nanoparticles as can be seen in table 3.

**Table 3: Recently developed Solid lipid nano particles using ultrasonication technique.**

Method	Drug	Lipid(s)	Surfactant(s)	Ref
Sonication	Lacitin 3147	Softisan 601	Kolliphor RH40 Transcutol P DMSO	[70]
Sonication	Nisin Z peptide	Softisan 601	Kolliphor RH40 Transcutol P DMSO	[71]
Sonication	Vitamin A	Stearic acid	Tween 80	[72]
Sonication	Ibuprofen or hydrocortisone	Witepsol	Sodium cholate Cremophor A25	[73]
Sonication	Curcumin	Cetyl palmitate	Tween 60	[74]
Sonication	Triamcinolone acetonide	Stearic acid	Soy PC Tween 80	[75]
Sonication	Pterostilbene	Compritol 888 ATO	Poloxamer 188 and poloxamer 407	[76]
Sonication	Rifampicin	Cetyl palmitate	Tween 80	[77]
Sonication	Vitamin A	Beeswax	Tween 80 Span 80	[78]
Sonication	Gliclazide	Compritol 888 ATO	Poloxamer 188	[79]
Sonication	Clozapine	Glyceryl behenate	Tween 80 Poloxamer 188	[80]
Sonication	Mitoxantrone	Cetyl palmitate	Tween 80	[81]
Sonication	Ascorbyl palmitate	Glyceryl monostearate	Pluronic F-68	[82]
Sonication	Mitoxantrone	Compritol ATO 888 Octadecyl amine	Tween 80	[83]
Sonication	Sulforaphene	Glyceryl monostearate	Sodium caseinate	[84]
Sonication	Simvastatin	Compritol 888 ATO	Gelucire 40/14	[85]

			Poloxamer 407	
Sonication	Dimethyl fumarate	Glyceryl monostearate	Poloxamer 188 Hydrogenated soy phosphatidylcholine	[86]
Sonication	Combination of Paclitaxel and photothermal agent IR-780	Tricaprin Cetyl palmitate	Pluronic F-68	[87]
Sonication	Cyclosporine A	Softisan 649	Tween 80	[88]
Sonication	Griseofulvin	Stearic acid	Chitosan	[89]

Abbreviation: DMSO, Dimethyl sulfoxide

### Solvent injection/Solvent evaporation

The lack of a sophisticated piece of equipment such as high-pressure homogenizer makes the solvent injection/evaporation technique more popular within small scale laboratories. This method involves the addition of the lipid phase solution to the aqueous phase solution heated to the same temperatures by the use of a syringe. The aqueous phase should be maintained at a controlled temperature with constant stirring or agitation usually accomplished by the use of magnetic stirrer. However, the use of an organic solvent usually; ethanol or methanol is required. Suitable methods or time is required until complete evaporation of the solvent [90]. One study done for the development of adapalene SLNs, injected the lipid solution at a constant flow rate [91] which is similar to the methods employed for the development of antifungal miconazole SLNs [92]. In contrast, in another study mometasone lipid phase was rapidly injected into the aqueous phase [93]. These different addition techniques and different stirring speeds and times allows modifications in preparation of the SLNs. Despite the initial stage of solvent injection, the use of sonication is usually used in combination to ensure stable nano sized particle production.

**Table 4: Recently developed solid lipid nanoparticles using solvent injection and/or solvent evaporation technique.**

Method of preparation	Drug(s)	Lipid(s)	Surfactant (s)	Ref
Solvent-evaporation	Cryptolepine	Stearic acid	Poloxamer 188	[94]
Solvent evaporation	Tacrolimus	Stearic acid	Tween 80 Sorbitan monooleate	[95]
Solvent evaporation	Microalgae omega 3	Softisan 649	Tween 80 Soy lecithin	[96]
Solvent injection	Prednisolone acetate	Compritol 888 ATO	Tween 80 Pluronic	[97]
Solvent evaporation	Cryptolepine	Stearic acid	Poloxamer 188	[98]
Solvent injection	Rhynchophylline	Glycerol monostearate	Tween 80 Solutol HS 15	[99]
Solvent evaporation	Naloxone	Glycerol monostearate	Pluronic 127 Tween 80	[100]
Solvent evaporation	Doxorubicin	Stearic acid Soy lecithin	Poloxamer 188	[101]
Solvent evaporation	Rapamycin	Compritol ATO 888	Tween 80	[102]
Solvent injection	Naringenin	Glyceryl tristearate Lecithin	Tween 80 Poloxamer 407	[103]



### Phase inversion

The phase-inversion temperature method is a low-energy approach for determining the solubility of polyethoxylated nonionic surfactants when temperatures vary. At high temperatures, the surfactant transitions from hydrophilic to hydrophobic, resulting in negative curvatures and water-swollen reverse micelles. At a certain temperature (the PIT temperature), the

surfactant has an affinity for both the oil and water phases, resulting in no spontaneous curvature and exceptionally low interfacial tension values. When the temperature falls below PIT, hydrated nonionic surfactants have high water solubility and produce fine droplets. The preparation of SLNs using phase inversion temperature technique is very limited within the literature with very few having successful outcomes [104].

**Table 5: Recently developed solid lipid nanoparticles using phase inversion method**

Method of preparation	Drug(s)	Lipid(s)	Surfactant (s)	Ref
Phase inversion temperature	Loratadine	Beeswax	Tween 80	[105]
Phase inversion Temperature	Querectin	Tripalmitin and/or Glycerol monostearate and/or Stearic acid	CRH 40 Kolliphor EL Tween 60 Tween 80	[104]
Phase inversion temperature/ sonication	benzo[k,l]xanthene lignans	Precirol ATO 5	Tween 80	[106]

### Microemulsion

The microemulsion or emulsification method was first introduced by Gasco in 1993 [107] Recent literature have used similar methods with various modifications. The production of oil in water emulsion is produced by melting lipid phase separately and heating aqueous phase with surfactant separately. The heated aqueous phase is then added to the lipid phase with continuous

stirring usually on a magnetic stirrer to produce an o/w emulsion. This emulsion is then added to cold water to produce a dispersion of SLN. The ratio of emulsion to cold water varies in literature and may range from a 1:10 ratio to 1:50 ratio, emulsion: water [108,109]. However, due to the low input of energy particles produced may not be as small as those compared to high pressure homogenization and other techniques.

**Table 6: Recently developed solid lipid nanoparticles using Microemulsion/emulsification methods**

Method of preparation	Drug(s)	Lipid(s)	Surfactant (s)	Ref
Solvent emulsion	Querectin	Glyceryl stearate Cholesterol lecithin	Tween 80	[110]
Microemulsion	Orobol	Capmul	Transcutol Labrasol	[111]
o/w Emulsion	Purpurin-18-N-propylimide methyl ester	Palmitic acid or Glycerol monostearate	Tween 20 or poloxamer 188	[112]
Emulsification	Dopamine	Glycerol tripalmitin	Tween 80	[113]
Microemulsion	Hydroquinone	Stearic acid	Tween 20	[114]
Microemulsion	Trans-ferulic acid	Compritol 888 ATO	Kolliphor EL Transcutol P	[115]
Double emulsion	Albendazole	Beeswax	Poloxamer 407	[116]
Solvent emulsification	Flurbiprofen	Stearic acid	Tween 80	[117]
Emulsification	Dopamine	Gelucire 50/13	Tween 85	[118]

Microemulsion	Isoniazid Pyrazinamide Rifampicin	Stearic acid Compritol 888 ATO	Poloxamer 188 Sodium taurocholate	[119]
Microemulsion	Lacticin 3147	Softisan 601	Kolliphor HS15 Kolliphor RH40	[120]
Microemulsion	Leflunomide	Compritol 888 ATO	Tween 80 Phospholipon 90G	[121]
Microemulsion	Chondroitin sulfate	Stearic acid Octadecylamine	Poloxamer 188	[122]
Emulsification	Resveratrol	Stearic acid Lecithin	Myrj 52	[123]
Emulsification	Nintedanib	Glyceryl monostearate Stearic acid Palmitic acid	Tween 80 Poloxamer 188	[124]
Microemulsion	Topotecan	Tricaprin	Tween 80 Span 20	[125]
Microemulsion	Amorolfine HCL	Stearic acid Monostearin	Sodium taurocholate Sodium tauroglycholate	[126]
Double emulsification	Tanespimycin	Precirol ATO 5 Glycerol Sorbitan monostearate	B-cyclodextrin Tween 80	[127]
Double emulsification	Combination streptomycin and hydroxychloroquine	Stearic acid Lecithin	Poloxamer	[128]
Double emulsification	Hydroxyzine HCL	Compritol 888 ATO	Soy lecithin Tween 80	[129]
Microemulsion	Chlorophyll	Trilaurin	Epikuron 200 Cremophor RH	[130]
Microemulsion	Econazole	Tripalmitic glyceride Glycerol	Tween 80	[131]
Emulsification	Resveratrol	Stearic acid Lecithin	Myrj 52	[132]
Double emulsion	Pralidoxime	Dynasan 114 Lipoid S75	Tween 80	[133]
Emulsification	Palmitoylethanolamide	Stearic acid Cholesteryl stearate	Span 85 Pluronic F68	[134]
Microemulsion	Docetaxel palmitate	Palmitic acid OR Stearic acid OR GMS OR Cetyl palmitate	Tween 80	[135]
Emulsification	Ambrisentan	Glyceryl monostearate	Tween 80	[136]

Abbreviation: HCL, hydrochloride



### Nano Spray Drying/ Others

Spray drying technique has been explored as a method to increase the stability of nanoparticles due to the aggregation of particles during storage in a dispersed solution, especially drugs that are highly susceptible to high temperatures and light. This method has been suggested to be a one step process, leading to reduction of costs during the processing steps. Major limitations to this technique include the tendency of the spray dried lipids to stick to surfaces leading to difficulties in recovering of the particles, coalescence and solid-state

transition of irregular lipid crystals produced by spray dry method. Although, reduction of particles to nano size may be achievable by spray drying method it is important to also consider the reconstitution properties of the dried nanoparticles. They should be able to be reconstituted with selected aqueous medium to the same nano sized particles without rapid agglomeration. Therefore, there are many factors that need to be considered before the optimum formulation is selected as final product. Factors as drying time, drying temperature, type and amount of lipid used and type and amount of surfactant used [137–139].

**Table 7: Preparation of Solid lipid nanoparticles using methods that are not as frequent**

Method	Drug	Lipid(s)	Surfactant(s)	Ref
Nano template engineering using micro syringe filter	Melatonin	Palmityl alcohol	Span 40 Tween 80 Myrj 52	[140]
Hot melt extrusion/ sonication	Tilmicosin	Carnauba wax	PVA or PVP or Poloxamer 188	[141]
Hot melt extrusion	Docetaxel	Glycerol monostearate	PEG 2000	[142]
Effervescent dispersion	Felodipine	Glyceryl behenate	Tween 80 Poloxamer 188	[143]
Supercritical	Hesperidin	Stearic acid	Tween 80	[144]
Microfluidic preparation	Trypsin or testosterone	Cetyl palmitate	Tween 80 Pluronic 68 Soy lecithin	[145]
Solvent diffusion	Rifampicin	Glyceryl monostearate		[146]
Solvent diffusion	B-carotene	Palmitic acid	Poloxamer 407	[147]
Thin film sonication	Curcumin	HSPC	PVP K15	[148]
Nano spray drying	5-Fluorouracil	Palmitic acid	PVA	[149]

Abbreviations: PVA, polyvinyl alcohol; PVP, poly vinyl pyrrolidine

### Combination methods

To overcome coalesces and increase the stability of nano emulsions, an innovative method by Glaubitt, introduced combination of a standard method of preparation of nanoparticles and spray drying. By combining ultrasound-assisted or high shear homogenization with spray drying it was assumed to increase the stability of the otherwise unstable long-term emulsions while

keeping the nano sized particles (preventing irregular crystals) [137].

Table 8 gives an indication of recent development of SLNs using combination of techniques. This proves that the use of more than one method is beneficial to overcome problems during the formulation of SLNs, whether the issue being stability, coalesces, preventing degradation and also to achieve desired nano particle size that may not have been achieved if prepared using a single method.

**Table 8: Recently developed solid lipid nanoparticles using a variety/ combination of methods**

Method	Drug	Lipid(s)	Surfactant(s)	Ref
Combination of double emulsion and melt dispersion	Ferrous sulfate	Monolaurin Stearic acid	Tween 80	[150]
Single emulsification and Double emulsification	Sodium aescinate	Glycerol monostearate Egg yolk lecithin	Poloxamer 188	[151]
Combination hot homogenization and sonication	Quercetin	Cetyl palmitate	Tween 80	[152]
Solvent evaporation/ emulsification	Mangiferin	Cholesterol egg phosphatidylcholine	Poloxamer 407	[153]
Solvent injection and homogenizer and sonication	Nystatin or fluconazole	Glycerol monostearate	Tween 80 Soy lecithin	[154]
Solvent evaporation/ sonication	Bimatoprost	Glycerol monostearate	Poloxamer 407	[155]
Emulsification/ evaporation	Morin hydrate	Glycerol monostearate	Tween 80 Soy lecithin	[156]
Emulsification/ sonication	Tolfenamic acid	Stearic acid	PVA	[157]
Emulsification/ homogenization and then Spray drying	Levofloxacin	Stearic acid	Tween 80 PEG 4000	[158]
Sonication/ homogenization	Paclitaxel	Stearic acid	Kolliphor 188	[159]
Emulsification/ sonication	Curcumin	Softisan 100	Emulmetik 900 Solutol HS 15	[160]
Emulsification/ sonication	Curcumin	Medium and long chain diacylglycerol or glycerol tripalmitate	Tween 20 or Quillaja saponin	[161]
Emulsification/ sonication	Beta hydroxybutyric acid, carmustine and temozolomide	Cetyl palmitate	Tween 80	[162]
Homogenization/ sonication	RVG-29 or Quercetin	Cetyl palmitate	Tween 80	[163]
Solvent emulsification/ sonication	Morin	Compritol 888 ATO	Tween 80 Phospholipon 80H	[164]
Microemulsion/ sonication	Mannose-6-Phosphate-Human serum albumin-matrine	Glycerol monostearate	Poloxamer 188	[165]
Emulsification/ sonication	Tetrahydrocurcumin	Glycerol monostearate	Tween 80 Soy lecithin	[166]
Solvent injection/ sonication	Paclitaxel or Sorafenib	Cetyl palmitate	Pluronic F68 Poly ethylene glycol	[167]
Homogenization/ sonication	Hesperidin	Precirol 5 ATO	Poloxamer 188 Span 80	[168]
Emulsification/ solvent evaporation	Gellan gum, Alginate and Nisin	Stearic acid	Poly vinyl alcohol	[169]
Homogenization/ sonication	Loteprednol	Precirol ATO 5	Tween 80	[170]

Emulsification/ solvent evaporation	Estradiol	Compritol 888 ATO Precirol ATO 5	Pluronic F127 Tween 80	[171]
Hot melt extrusion/ homogenization	Alprazolam	Compritol 888 ATO	Tween 20	[172]
Emulsification/ high pressure homogenization	Vitamin D	Precirol 5 ATO	Tween 80	[173]
Emulsification/ sonication	Budesonide	Compritol 888 ATO	Sodium cellulose sulphate	[174]
Emulsification/ solvent evaporation	Phytol	1,3-distearyl-2-oleyl glycerol	Poly vinyl alcohol	[175]
Double emulsion/ solvent evaporation	Gemcitabine	Glycerol monostearate	Soy lecithin Pluronic F127	[176]
Homogenization/ emulsification	Retinol and Pentapeptide-18	Glyceryl monostearate, hexadecyltrimethylammonium, L-phosphatidylcholine	Tween 80 Sodium cholate	[177]
Homogenization/ sonication	Cannibidiol	Glyceryl mono stearate	Tween 80	[178]
Homogenization/ sonication	8-Methoxypsoralen	Compritol 888 ATO	Poloxamer 188 Transcutol P	[179]
High pressure homogenization/ sonication	Verapamil	Stearic acid	Poloxamer 188	[180]
Homogenization/ sonication	Amiodarone	Witepsol W 35 Glyceryl monostearate	Poloxamer Sodium lauryl sulfate Soy lecithin	[181]
Double emulsification/ sonication	Vildagliptin	Stearic acid	Tween 80 Span 80	[182]
Homogenization/ sonication	Atorvastatin calcium	Compritol 888 ATO Lipoid S100	Gelucire 50/13	[183]
Homogenization/ sonication	Metformin	Glyceryl monostearate	Span 60 Tween 80	[184]
Emulsification/ evaporation/ sonication	Sunitinib	Glyceryl monostearate	Tween 80 Span 80	[185]
Emulsification/sonication	Gefitinib	Stearic acid	Pluronic F-68	[186]
Homogenization/ sonication	Kojic acid	Glyceryl monostearate Cholesterol	Span 60 Tween 20	[187]
Solvent injection/ sonication	Atorvastatin	Glyceryl monostearate	Tween 40 Span 80	[188]
Emulsification/ evaporation	Valsartan	Glyceryl monostearate Egg lecithin	Poloxamer 407	[189]
Emulsification/ sonication	Mirabegron	Glyceryl monostearate	Tween 80	[190]
Homogenization/ sonication	Caffeic acid	Compritol 888 ATO	Tween 80 Pluronic F127	[191]

Emulsification/ solvent evaporation	Combination Amphotericin B and paromomycin	Glyceryl monostearate	Tween 80 Soy lecithin	[192]
Double emulsification/ sonication	Insulin	phosphatidylcholine	Poloxamer 188	[193]
Sonication/ film dispersion	Combination curcumin and paclitaxel	Hydrogenated soybean phospholipids	Polyvinyl pyrrolidone k15	[194]
Microemulsion/ homogenization	Bedaquiline	Capmul MCM C10	Phospholipon 90G Poloxamer 188	[195]
Homogenization/ sonication	Acyclovir	Compritol ATO 888	Tween 80	[196]
Solvent evaporation/ homogenization	Metronidazole	Precirol ATO 5	Tween 80	[197]
Homogenization/ sonication	Foeniculum vulgare	Stearic acid	Phosphatidylcholine Tween 80	[198]
Emulsification/ homogenization	Naringenin	Glyceryl monooleate	Tocopheryl polyethylene glycol succinate	[199]
Homogenization/ sonication	Rifampicin	Glycerol tripalmitate	Tween 80	[200]
Emulsification/ sonication	Alpha-asarone	Precirol 5 ATO Palmitic acid	Gelucire 53/13 Tween 80	[201]
Emulsification/ solvent evaporation	Perphenazine	Glyceryl monostearate Lecithin	Tween 80	[202]
Homogenization/ sonication	Combination of Docetaxel and erlotinib	Precirol 5 ATO	Tween 20	[203]
Solvent injection/ homogenization	Oxiconazole nitrate	Tyloxapol Stearic acid	Tween 80 Poloxamer 407	
Homogenization/ sonication	Paclitaxel	Precirol 5 ATO Stearic acid	Tween 20 Poloxamer 407 Soy lecithin	[204]
Solvent injection/ sonication	Acyclovir	Stearic acid	Tween 80	[205]
Emulsification/ solvent evaporation	Curcumin	Stearic acid	Myrj 52 Soy lecithin	[206]
High Pressure homogenization/ sonication	Capsaicin	Compritol ATO 888 OR Glyceryl monostearate AND Cetyl alcohol OR Stearyl alcohol	Span 80 Tween 80	[207]
Emulsification/ sonication	Brigatinib	Stearic acid	Soy lecithin	[208]
Homogenization/ sonication	Gabapentin	Cholesterol OR Stearic acid	Tween 80 OR Pluronic F-68	[209]
Homogenization/ solvent evaporation	Beta sitosterol	Compritol ATO 888	Phospholipon 90G Tween 80	[210]
Emulsification/ solvent evaporation	Letrozole	Tripalmitin glyceride Octadecylamine	Tween 80	[211]

Emulsification/ sonication	Insulin	Compritol ATO 888	Soy lecithin Poloxamer 407	[212]
High pressure homogenization	Bromelain	Stearic acid Tristearin	Tween 80 Span 80	[213]
Emulsification/ solvent evaporation	Curcumin	Stearic acid	Myrj 52 Soy lecithin	[214]
Homogenization/ sonication	Lavender oil	Cholesterol Lecithin	Tween 80	[215]
Emulsification/ solvent evaporation	Delafloxacin	Stearic acid	Pluronic F-127	[216]
Emulsification/ solvent evaporation	Cilnidipine	Compritol ATO 888	Poloxamer 188	[217]
Homogenization/ sonication	Penicillin	Compritol ATO 888	Lutrol F68	[218]
Homogenization/ sonication	Paclitaxel	Precirol 5 ATO Stearic acid Lecithin	Tween 20 Poloxamer 407	[219]
Emulsification/ homogenization	Cannabidiol	Compritol ATO 888 Witepsol E85	Tween 80 Poloxamer 188	[220]
Emulsification/ sonication	Combination of curcumin and Lawsone	Cetyl palmitate	Polyethylene glycol 400	[221]
Emulsification/ sonication	Abemaciclib	Precirol 5 ATO	Brij 58	[222]
Emulsification/ sonication	Acalabrutinib	Compritol ATO 888 Stearyl palmitate	Tween 80 Poloxamer 188	[223]
Homogenization/ sonication	Vancomycin	Compritol 888 ATO	Luro F68	[224]

Abbreviation: PVA, poly vinyl alcohol

## Conclusion

Development of drugs incorporated with SLNs have been widely explored within recent years. They have been used for specific drug delivery/targeting. Many methods with modifications of each method have been explored depending on specific needs and requirements of the final SLN. The nano size of SLN have found to have advantages within literature but further exploration is required, in addition although SLN have been described within literature very few have been patented and available within the market. Although there have been some formulations described, investigations within preclinical and clinical trials make the use of drug incorporated within SLN a promising future in drug delivery.

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