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Review Article

# A REVIEW ON THE APPLICATION OF SOLID LIPID NANOPARTICLES IN TRANSDERMAL PATCH DRUG DELIVERY

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**ABSTRACT**

The transdermal patches are used to deliver medication through the skin to treat the entire ailment. These depend on a unique size property of skins to encoded drugs solid lipid nanoparticles (SLNs) current a chance to create upon novel therapeutic properties used for drugs transmission SLN targeting holds great potential for target achieving, a penalty area, Many aspects of the loaded of SLN sin transdermal patches for increasing mechanism of penetration, formulation, characterization parameters, future advantages, limitations of SLNs, had better biocompatibility, low harmfulness, SLNs is physically stable, and better delivery for Lipophilic drugs are discussed here. SLNs are a hybrid of liposomes and polymer-based carriers that could be used to encapsulate both lipid and water-soluble medicines. SLN is a low-cost product that can be scaled up. They also have a long-life span and could be customized by using different lipids. Because of their multiple significant qualities, SLNs also started to emerge when effective drug delivery carriers, as well as the prospect with liposome delivery of drugs, depends heavily on them. Many patents relating to SLNs have already been submitted, there are more invented SLN-based delivery systems on the way soon.

**Keywords:** Transdermal patches, solid lipids nanoparticles, colloidal, targeted drugs delivery.

## INTRODUCTION

The first patches were available in the market were approved by (USFDA) in December 1979. Scopolamine in these patches administered for nausea and vomiting associated with motion sickness [1,2]. Transdermal patches were first introduced by Alejandro Zaffaroni was a biotechnology innovator that early worked in controlled drug delivery preparation, his idea only for transdermal patches, thus increasing the rate for research into advanced drug delivery systems. In 1910 SLNs were introduced which brings an excellent revolution within the sector of medication delivery due to several influenceable properties within the sector of formulation development [3]. Solid lipid nanoparticles (SLNs) were developed in 1991 to produce biocompatibility, storage stability, and preventing the consolidated medication from decay [4]. In 2001, the transdermal patch market in the United States approached $1.2 billion. It must have been predicated on 11 therapeutic agents: opioids, ammonium nitrate, estrogen, ethindroneacetate, testosterone, and neither, clonazepam, cannabinoids, morphine, and prazosin [5]. Until 2003, the FDA had accepted more than 13 transdermal patch products.

Nitroglycerin pads have been used to treat angina in situ so instead of sublingual pills [6]. Permeation ergot alkaloids were frequently used for kinetic studies [7]. Clonidine drugs were available in pad form used for anti-hypertensive [8]. Emsam was the MAOI selegiline in the form of transdermal, develop first transdermal delivery agent used such as an antidepressant methylphenidate in 2006 [9]. Daytrana the primary deficit hyperactivity disorder (ADHD) as a transdermal delivery system, was approved through the FDA in April 2006 [10]. Cyanocobalamin also administered through a patch, was compatible with transdermal patches [11]. (5-HTP) could be ordered through a pad, it was cast in the UK earlier in 2014[12]. Rivastigmine, a Parkinson's disease treatment medicine, had been introduced in 2007 under the brand name Exelon [13]. The twice newly approved transdermal patches (a contraceptive patch containing Ethinyl estradiol or even norelgestromin or an enlarged prostate patch containing oxybutynin)[14]. SLNs, colloidal bearer of the nanoscopic range was (50–1000nm), fabricated from solid lipids, are advance to beat such as polymer degradation and the quality of toxic to cells, lack of an appropriately huge-scale preparation method, inferior stability, drug aperture and fusion, phospholipid demotion, great value, and sterilization problems of classical colloidal carriers [15]. Nanotechnology studies and use of size range 1-1000nm [16]. Nanotechnology is very important for drug delivery systems using particles are nanoparticles, nanosuspension, nanoemulgel, nanotubes, and nanocrystal [17]. SLNs display different special features like minor toxicity, wide area, control drug release, remarkable reflected or transmitted in comparison to common carriers, and also the ability to improve medication absorption and stability [18,19]. Sudden discharge of a drug from pad gamble on the original type of drug location within the preparation. SLNs formulate from biodegradable and biocompatible factors can merge one and the other hydrophilic and lipophilic pharmaceutical actives medicine hence developing to do a possible option for prolonging and targeted drug delivery [20]. The SLNs had a solid core of hydrophobic with a phospholipid of monolayer coating then the drug was commonly discharged or diffuses within the effective origin.

**Transdermal Patch**

Topically administered medicaments through transdermal drug delivery arrangement [20]. Pad is the pharmaceutical formulation of irregular sizes, have one or more effective ingredients expected elected tested After passing through the skin barriers, an active substance is delivered to the bloodstream via the unbroken skin. It's indeed possible to bypass the first-pass achieved. Thus, the drugs deliver into the bloodstream at a fixed and prolong release rate. That diffusion process changed; the drug directly introduces the bloodstream precisely through the skin layer. yet a more concentration in the patch and a low concentration within the blood. The drug will keep diffusing into the blood from higher concentration into the lower concentration for a protracted duration of it slow is require care of the regular percentage of drug within the bloodstream or blood circulation. To the main limitation of the pad system from the very case that the skin is an incredible use full barrier, at the time that a result only medication, whole molecules can be sufficiently little diffusion to the skin was pass by this method. The transdermal patches have various components.

**Type of Polymer Chart**

**Polymer matrix**

It was considered as the backbone of the transdermal patches, which prolong the leak of the drugs through the device [21]. To make an ideal patch the polymer should have severed properties, the given below factor that considered the polymer that can be used in the skin patch.

- It goes not decompose on storage /or it should be stable.
- A polymer was chemically inert.
- A polymer was non-toxic.
- A polymer could be cheap.
- It can be easily manufactured.

**Drug**

The drug's solution directly in contact with skin patches Drugs with extensive first-pass metabolism, such as nitroglycerine, benefit from a narrow therapeutic window.

**Physiochemical properties**

a. Drugs should have a low melting point.
b. The drugs keep having to lean in both the lipophilic and hydrophilic phases.
c. The drugs gain a molecular weight of less than 1000 Dalton.
d. The drugs should be clear /white in color.
e. The drug dosing frequency once in day/weak.
f. The drugs should be easy to remove and apply.

**Biological properties**

a. The drugs do not produce an irritant response.
b. The drugs [t1/2] obtain short.
c. The drugs should be potent.
d. The drugs are not established in the transdermal patches zero-order release profile.

**Permeation Enhancer**

Polymer and/or substance which help to increase the permeability of the stratum corneum Chemical permeation enhancer [cpes] are molecules that interact with the constituent of skin. The flux of drugs transport equation should be given below.

$$J = -Ddc/dx$$

J-flux
The coefficient of D-diffusion
The diffusing specters' C-concentration
X-spatial coordinates are a type of coordinate system.
The negative sign in the Fick low diffusion that the direction that the concentration decrease.

**Solvent**

The compound which increases the permeation possibly by swelling the polar pathway Ex-methanol, glycol.

**Surfactant**

There is the compound having lower the surface tension and/or interfacial tension between two liquids via modified the permeation expected the length of the hydrocarbon chain is determined by the polar head group and the length of the hydrocarbon chain. Anionic surface, Diacetyl sulphosuccinate.

1. Non-ionic, Pluronic F127.
2. Bile salt, Sodium Deoxycholate.

**Miscellaneous chemical**

Enhance the permeation increase. Ex-urea, calcium, thioglycolate.

**Adhesive**

The adhesive was a critical factor to be considered because; it was directly related to the drug delivery, the back of the device, and the therapeutic effect.

1. It must not be irritant.
2. It has easily been removed.
3. It has not permitted a residue on the skin.

**Different type of skin patches**

1. Multi-layer drugs in adhesive.
2. Drugs reservoir in adhesive.
3. Drugs matrix in the adhesive.
4. Single-coated drugs in adhesive.

**Adhesive Single-layer drugs**

The system also contains drugs and it is an adhesive layer, during the adhesive layer on a patch does more than just stick a various piece around each other; it also runs the length of the structure via the skin however more important layer was enclosed by a short-lived lined and an endorsement.

**Multi-layer drugs in adhesive**

The system is the same as for single-layer drugs in adhesive, but it added one more coat of drugs in adhesive mostly separates the sheath yet not altogether cases [22]. The particular layer was furthermore as actual release of the drugs and addition sheet for prolonged-release this patch also had a short-lived liner from the reservoir, along together with long-lasting adherence. The rate of drug molecule release is affected by membrane permeability and diffusion.

**Drugs reservoir**

In adhesive affecting a special-coat along with multilayer drugs into the adhesive system, separate the drugs layer from the transdermal system have a reservoir. It has a liquid compartment containing a drug solution or suspension that is separated by an adhesive layer [23]. The drug reservoir was exactly encapsulated current requiring compartment model taken away drugs-impermeable metallic plastic laminate, by the amount regulating membrane invented of the polymer such as vinyl acetate, that patch was approved away the helping layer, the current system release rate was zero-order.

**Matrix**

This system has a semisolid matrix coated with drug; It is also referred to with a monolithic device. Here patch surrounds the effective drug layer moderately overloading on it.

**Vapor patch**
Here the system form about patches the adhesive layer was not at all alone found via server adhesive to the various layer together but also release vapor, they are only new in the market which discharges essential oil within 5 h, which was generally need in case of mass and some new vapor patches are available in the retail to enhance the quality of cigarettes by using one smoke in a month.

**Transdermal permeation**
The topical membrane was the most complete only usable organ if the fraction of the tissue separated in millimeter small the body, it was surface taken away basic network. Different steps that involve the transit of drugs through the patch in the bloodstream are as follows.

1. Dispersion taken away from drugs rate-limiting membrane into the stratum corneum.
2. Dispersion of drugs from drugs reservoir through rate-controlling membrane.
3. The dermal papillary layer is made up of a capillary network that works to drug intake.
4. Absorption by stratum coronium and diffusion over the viable epidermis.
5. Response at mark unit.

**Colloidal drugs delivery system**
Colloidal drug delivery systems [CDDs] are nanometer particle diameter application designs. It is critical in the efficient transportation of loaded drugs to the marking unit [24]. Colloidal drugs carrier was better significant body permanently needed being successful transportation of loaded drugs, which is included as nanosphere, noisome, liposome, multiple emulsion. They were drugs vector which confiscates, transport as well as keep to the active drugs to the route, at the same time rinsed or pass it within or within the vicinity of the target. While therapeutic effects must be attained during administration, undesirable toxic effects should be decreased. The consumption of long-term drugs and reactions must be minimized naturally by adhere the chemical agent within the unhealthy region. Essentially not required overdose. This system was selected for reduces the fundamental effect to excellent quality. Nanocarrier such as liposomes and nanoparticles in Colloidal drugs carrier is modified the delivery of a substance must be being used to boost the therapeutic index of medication to increase their efficacy, colloidal like the micellar solution, vesicle, and liquid crystal dispersion, nanoparticle dispersion [05-400] diameter [25]. That drug delivery system shows great promise. Advance technique is used to developing the preparation, the rationale is to get the system to improved drug loading and releasing properties furthermore as well as self-life as minimum toxicity, so that microstructure of a system that the matrix drugs properties had been influenced because of molecular interaction, exclusively those drugs which are amphiphilic and/or mesogenic properties get a pass.

**Characteristics of an ideal CDDS**
Optimal colloidal-drugs carrier is going to rocket science must the following feature.

1. It has to pass the anatomical barrier.
2. It should especially identify and select the target cell, control the avidity, particularly of surface ligands.
3. A ligand of drugs and operate the unit must stable in the plasma.
4. Carrier particles should be non-toxic and biodegradable or macromolecular, after concession also internalization.
5. Modules are used as carrier navigation Otherwise, CDDS will cross over the site if site recognition is not ubiquitous, the concept of targeting is overpowered.

**Classification of colloidal drugs carriers CDDS could be classified as follow**s:

| | |
|---|---|
| **A. Vesicular system** | Liposome, niosomes, pharmacosomes, virosomes, immunoliposomes. |
| **b. Microparticulate system** | Microparticles, nanoparticles, magnetic microspheres, albumin microsphere, nanocapsules. |

**Application of CDDS**

1. Colloidal drug carrier provides an expansion of benefits in a variety of delivery system, as weakly soluble compounds. Colloidal carriers' first generation, however, possesses a variety of limitations so neglected to be considered to be used in drug delivery as the carrier, mainly observed in liposomes and submicron-sized lipid emulsion. A choice colloidal delivery system in a variety of solid lipids proposed based on melted emulsion nanoparticles. Physicochemical characterization presented that these where not only emulsions must solidify in nature.

2. Liposomes and nanoparticles are a Colloidal drug carrier had accustomed enhance the therapeutic index in traditional and current drugs by customized their distribution, so that developing their efficacy also minimizing their toxicity. The examination of the physicochemical characteristics of a drugs dispersion would then be followed by the examination of a transporter. Specially designed for the target yet the mechanism of action, one solution that must be provided is an innovative grade of active drug ingredients, such as protein molecules, alleles, and an oligonucleotide. Individuals have provided a variety of transportation methods in the form of other novel drugs.

3. Treatment of tuberculosis (TB) through Nanoparticle-based drug delivery systems. The aqueous suspension is colloidal from which crosses the skin barrier alone through hydrophilic pathways. thin pore spaces with specific sets inside the surface and influencing noteworthy nano-pores inside the skin as impediments modelling.

4. Engineering drugs themselves in nanoparticles drugs in nanoparticles had also emerged as a replacement approach for the delivery of hydrophobic drugs. Nanoparticles and nanocomposite had been applying as drug delivery systems with huge achievement; moreover, nanoparticle as long as a drug delivery which is greater potential for several applications, immunodeficiency syndrome (AIDS) treatment, cancer therapy, through providing proteases, medications, virostatics, vaccines, and as vesicles to cross the blood-brain barrier.

5. Polymeric carrier for water-soluble and amphiphilic drugs. These micelles are significantly more stable than surfactant micelles and have the potential to solubilize significant quantities of nonionic surfactants throughout their internal structure. cause of their hydrophilic shell and small size, they frequently have controlled associated with the occurrence in vivo and may acquire in cancer cells.

**Solid lipids nanoparticles**
These are the tiny number of active pharmaceutical ingredient [API] which is under developing stage, had reduced water solubility and reduced bioavailability. Achieving desirable bioavailability was no easy task, hence to overcome the biggest complication nanotechnology was one of the modern, novel approaches in the field of drugs delivery, medical science, and formulation of the unique in tiny size and huge surface area, high drugs loading capacity as well as the interaction of phase at

interphase these are attractive in nature as long as their potential to boost the production of pharmaneutraceuticals and other material like cosmetic also, it was physically stable [SLNS]are novel lipids based nanocarrier having size range between 10-1000 nm with the help of [SLNBs]. Then it was possible now to formulate controlled release and site-specific drug delivery [15]. They have several advantages of a traditional system and avoid the major disadvantage. In the last decade, SNS is the colloidal carrier development as a different system to the current conventional carrier/gel, nanotube, polymeric nanoparticles, and lipid-based carrier, etc. while must have good compatibility, narrow toxicity, and lipophilic drugs are improved and discharged through SLNs. Hence SLNs hold good assure for releasing the goal of control and site-specific drug delivery having desirable bioavailability due to which attracts the wide attention of researchers. Advantage of SLN controlled rate/stability drugs release in specific site drug delivery. SLN is not suitable for a cell of the reticuloendothelial system (RES) because of nanosized ranges, therefore, they are able to avoid spleen and liver filtering because they are able to avoid liver and spleen purification [26,27]. probability of incorporation both hydrophilic and lipophilic drugs and row material necessary as same as emulation, prolong stability and drugs by lyophilization was achieved and easy to scale up and sterilizer affordable and biocompatible and biodegradable composition ingredient [28], a major step towards a drugs product with improving patient acceptability and compliance had been made as a major disadvantage of the commercial formulation are closely packed lipid matrix network, being narrow space for drugs encapsulation, thus poor drugs loading capacity [29,30]. Probability of these drug expulsion under polymeric transition drug warehouses [31,32]. This dispersion having a type of huge percentage (70-90) % water content [33] and particle growth as well as broad size distribution [34,35].

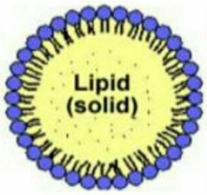


**Figure 1: Structure of solid lipid nanoparticles (SLN)**

**SLN's in transdermal patches**

We know that there are several limitations with conventional dosage forms, such as low permeability, degradation by gastrointestinal enzymes, irregular absorption, fluctuation in drugs plasma level, drug degradation first-pass metabolism and so varied which finally affects the therapeutic efficacy of drugs. To defeat these problem SLNs in transdermal patches these are one of the most suitable and conventional dosage forms these are convenient to use and increase patient compliance [36]. SLNTP not only avoids the first-pass metabolism but also enhances the permeation of drugs through the skin which directly acts on this site of action. This was a predetermined rate, that ultimately leads to an increase in the solid-liquid matrix and avoids it from chemical or physical degradation increase the drug loading was possible with SLNs ultimately decrease of the dosage frequently. In the general province of unconsciousness drugs can be delivered to the patient. It was not found to be possible with the tablet and /or capsules. Transdermal patches and easy to use and do not need any type of special help and they are loaded with SLN*s t*hey provide furnish in dermal therapeutic effect.

**Preparation of solid lipids nanoparticles**

SLN preparation from lipoids, emulsion, and solvent by using different method given below [37].

**Technique of preparation of solid lipid nanoparticles**

**High pressure homogenization**

This technique was powerful and dependable; it was used in the manufacturing of SLNs. It pushes a fluid pressure [2000br] through a thin hole. The liquid accelerates on a very short distance to a very high velocity [greater than 1000km/hr] very high [vh] shear stress at room temperature [38]. The main factor the particle size in submicron ranges more after [5-15] % and the lipid content up to 30% lipid content has been investigated, this can have a couple of hot and cold homogenization, work in the construction of mixing the drugs in the bulk of lipid melt.

**Hot homogenization**

This homogenization was carried out above the melting point of the lipids, so that known as the hot homogenization of an emulsion by the high loaded lipid melt and the aqueous emulsifier phase was obtained. In general, high temperature results in a reduction in particle size due to the decreased viscosity of the aqueous phase. Increase high temperature the degradation rate of the drugs as same as the carrier. Increase homogenization pressure and/or the number of rotations result in a decrease in the particles' size because of the high kinetic energy in the particles. The colloidal hot oil in water emulsion was formed after homogenization, which upon cooling causes the crystallization of the lipid in globules and leads to the SLPs [39].

**Cold homogenization**

This homogenization has been generated to get the better various issue associated with hot homogenization like temperature causes drugs degradation the distribution of the drug patterns production of supercooled melt. In this method, the drugs load lipid melt was cold to reduce. Solid lipids into lipids microparticles and these lipids microparticles are dispersed in the coldest surfactant solution to produces a pre-suspension was homogenized at room temperature. The gravitational force was strong enough to break the liquid microparticles into solid lipid nanoparticles. Particle sizes attained by this technique are usually in the range of 50-100nm [40].

**Solvent evaporation**

In this method, lipophilic material was dissolved in a water-immiscible organic solvent Ex-cyclohexane, ethanol. It was emulsified in an aqueous phase then evaporated off the solvent. Nanoparticle dispersion was formed with the help of precipitation of the aqueous medium by producing nanoparticles of 25nm in size ranges. Nanoparticles preparation by this blueprint are used to nano-size, non- flocculated (single entity), there was a high entrapment efficiency [41,42].

**Microemulsion base method**

This method is depending on the dilution of the microemulsion, it generally defines as microemulsion is two type systems, and it lies an inner and outer phase. The hot microemulsion is scattered in cold water by stirring fluid. Such as tablets, pills, capsules, through the granulation process but in the case of low particle content, too much moisture needs to be removed. High-temperature gradients cause rapid lipids crystallization and prevent accumulation with the help of the dilution step. The predictable lipids content was much lower as compared with the HPH based formulations. The dilution process was critically determined by the composition of the micro emulsion [43].

**Spray drying method**
This method was another substitute to the lyophilization process that indicates using lipids with such a transition temperature greater than $70^0$ C [44]. The SLNs concentration of 1%in a solution of 30%trehalose in water 20% and/or the trehalose-eater ethanol-mixture [10/90v/*v*] could be used; the two best results to get the form particles aggregation due to high temperature and shearer force, particles melt of the particles, and these are drawback associated with this method [45].

**Double emulsion method**
The hydrophilic drugs are encapsulated with a stabilizer or surface-active agent [46], this method is known as a multiple emulsion method. It has three basic steps, a. preparation of the w/o emulsion or inverse emulsion, b. addition w/o emulsion into the aqueous solution of polymer or surfactants into an emulsion $w_1/o/_{w2}$ emulsion with keep stirring through [(water bath) sonication, homogenization] and, c. evaporation of the solvent or filtration of the multiple emulsion from the nanoparticles. This technique produces large size-particle them surface modification is achieved through this technique by incorporating hydrophilic polymer such as PEG drugs, b. step [47].

**Lyophilization**
It increases the physical and chemical stability of SLN's and over prolongs the period, then it prevents degradation response and prevents the initial particle size, SLN's ingredients are required for increasing chemical strength and narrow size distribution of particles to circumvent crystal growth. The SLN's product should be unaffected by temperature, humidity variation during transportation. It was an aqueous SLN dispersion, particles size had not to change variation over several months, and it involves surfactant protective effects where the lipid content of SLN dispersion should not excess 5% for avoiding the increase in particle sizes [48].

**Ultrasound dispersion in film**
The lipids and also the drugs were put into a suitable organic solvent, after decompression, rotation, and evaporation of the organic, a lipids film is made, then the solution. This includes the emulsion was added, The SLN with uniform particle size is obtained by using the ultrasound with the probe to diffusion.

**SLN Evaluation**

**Drugs content uniformity determination**
Every formulation from three films was taken separately and in a different 100ml volumetric flask, 100ml with phosphate-buffer solution (6.8) has been incorporated as well as consistently mixed for twenty-four-hour then the solution was filtered, absorption was measure later suitable dilution and analyzed in UV spectrophotometry (U-1700 CE, Shimadzu Corporation, Japan).

**Percentage moisture content**
A percentage water uptake test was performed to evaluate the film's stability and probity in high temperature conditions; Individually weigh the film and place it in the $CaCl_2$ at 25 $^0$C/ 77 F. The film weighted a different interval of 24,36,48 through out that time. They have a consistent weight. This formula determines the percentage of moisture contained.

**In-vitro release testing**
Dissolution studies are administration in a very USP dissolution apparatus using 900ml of dissolution, medium at 37±0.50c, and a rotation speed of fifty rpm was used. And aliquot of sample is periodically withdrawn and replaced with fresh medium. The samples were filtered Whatman paper and analyzed spectrophotometrically.

**Transdermal Patches Containing Solid Lipid Nanoparticles**

**Membrane penetration – a managed system**
Transdermal Nitro, for example, is a multilaminate process. It is made up of three parts that are held together by two layers of drug-containing SLN adhesive. Initially, this same medication SLN had been transformed into the chemical and physical demonstrate knowledge for incorporation into the product; make the uniform solution dissolve in a solvent. Removal of the solvent, there is a skinny film because of adhesive compositions.

**System of adhesive dispersion**
The preparation process could be classified into the following.
a. Formation of solution with the individual matrix.
b. Formation of stock solution with the help of Raw material by dissolved in an organic solvent.
c. Matrix solution was ready for the stock solution.
d. The effective SLN, and other non-soluble excipients are added.

**Individual matrix layer coating**
Separate layers are formed by coating a remedy and separating a solvent besides soaking through the adhesive device.
(A) The film crews.
(B) A unit for drying clothes.

(A) The film crews
Preparations were indeed encapsulated with solvent, as well as the matrix solution is determined by viscosity, solid content, flowability, and surface tension.
(B) A unit for drying clothes
Each solvent was evaporated first from coating density through running a wrapped site through a transport system similar to the rolled screw, conveyer belt.

**System with matrix diffusion control**
Each polymer used for the medication was mostly mashed with Polyvinyl chloride in an organic solvent, and also the finely ground waxy matrices were prepared by dissolving the medication throughout liquid fat followed by coagulation, and the flakes had been compressed into the tablets. A drug diffuses out from the gum because of swelling.

**The SLNP-Transdermal Patches Have Been Evaluated**

**Physical appearance**
Individual visual examinations were performed on all of the formulated patches for color, clearness, adaptability, and softness, texture.

**Drug Content Uniformity determination**
Pieces of 3x3 size were cut from each preparation and placed in a 100 ml volumetric flask with 100 ml phosphate-buffered saline at PH 6.8. The content was magnetically stirred for 2.5 h. Then the solution was filtered with the help of Whatman filter paper (0.45μ), dilute appropriately, and analysed on a UV spectrophotometer the absorption values, drug content was determined.

%Drug loading =the amount of entrapped drug in SLN /The total weight of SLN X 100

**Folding Endurance**
The formulations were conducted in order to test each plasticizer's productivity even as formulation quality compares using different polymers. The Folding endurance was measured through hand operating and repeated folding at a tiny strip of the patch (3x3) at the same place before it was broken. The number of times the film

was folded at the same places without breaking also creaking that the folding endurance value.

**The patch thicknesses**
The film thickness must have been measured using a screw gauge at various points just on film, and the ordinary mean value and deviation values to the different readings had all been determined by calculating while the drug-loaded film was being measured.

**Uniformity of weight**
The weight variation test through weighing every patch assistance at a digital balance. The average values were calculated.

**Percentage moisture content**
To check the stability and probity of the film in elevated hot temperatures, a percentage moisture absorption test was performed, in which the film was weighed individually and placed in $CaCl_2$ at 25 $^0$C/ 77 F. The film weighted a different interval of 24,36,48 during this time. They have a consistent weight. the percentage of moisture contained as determined by this formula moisture content in percent.

$$\%\ Maximum\ moisture\ = \frac{Total\ drug - Final\ mass}{Final} \times 100$$

**In-vitro release testing**
The Franz diffusion cell was used to describe transdermal preparations in vitro; this method was stable for the indicator of drugs that deliver over the skin for topical preparation. The Franz diffusion cell was filled with 50ml of buffer solution PH7.4 then in vitro release study was taken out with the help of synthetic cellophane membrane, cellophane membrane as a donor chamber which carried formulation then the assembly was regularly sustained at 37.0 ± 2.0 °C at 50 rpm. The sample was withdrawing at a relevant period (0.5, 1, 1.5, 2.5, 3.5, 6, 12, and 24 h) with a volume of buffer to keep the receptor development stage quantity at 50 ml. The sample was examined using a spectrophotometer [49].

**Ex-vivo permeation study**
Drug permeation studies were applied in Franz diffusion cell the rat skin specified in size is mounted carefully removed and washed with saline. The skin store for 5 h. donor solution consisting SLN containing drugs [127]. The receiver compartment of Franz diffusion was crammed with 50ml of buffer PH 7.4 the assembly temperature at 37 ± 0.50 °C and stirring rate control at 600 rpm. sample (1 ml aliquots) of the medium withdraw at the determined period and replace the sample of the same amount to maintain the phase volume to 50ml. Every sample was filtered and analysed to the spectrophotometer.

**Flatness study**
It was studied for the quality to prepare the transdermal patches to maintain a smooth surface also they should not cramp with the period. Slices had been chopped from of the film at various points. Measure the length of the film and deviation in length due to uniformity dot maintain in flatness through determining % narrowing along 0% narrowing equal to 100% flatness. Determination of flatness by this formula $(I_1\text{-}I_2)/I_1$ x 100% hence $I_1$was initial length, $I_2$was the final length of all film.

**Surface pH**
Double distilled water 0.5 ml was taken in a glass tube then patches pour into a tube for 1 h and allow swelling. The PH measurement glass electrode had been directly connected to the patch's surface, and readings were taken at 1-minute intervals.

**Characterisation technique of SLNs**
Characterization's technique which needs to determine the various parameter of SLNs, such as Zeta potential, size as well as particle size distribution, degree of crystallinity, polymorphism changed by lipid modification [50].

**The size of the particles and their zeta potential**
Electrophoretic mobility was determined by Zeta potential through Malvern Zeta-sizer Nano 90 Malvern instruments, UK. The strength range of 25 V cm-1 was enforced. Following use, each formulation was diluted in water. The main characteristics of SLNS are the polydispersity index (PDI), magnetic properties, and zeta size [51]. Dynamic light scattering (DLS) was one of the most effective methods used it to classify solid lipid nanoparticles. this method was used to improve the preparation along with study and sensitivity to sub-micrometer particles [52]. Physical stability was the more important factor scale of SLNs [53]. The thumb rule is that high zeta potential values (e.g., greater than 30 mV) combined with negative charge can stabilize colloidal dispersion [54]. Regulation and verification of nanocarrier formulations are thus useful for successful clinical prospects [55].

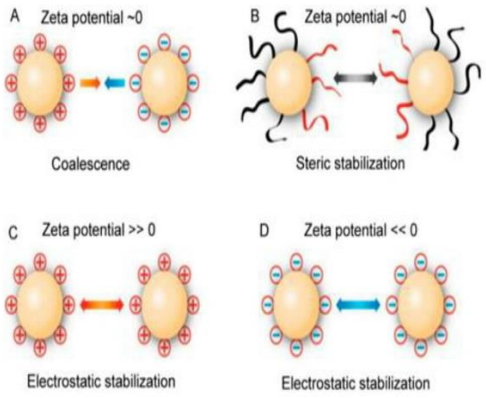


**Figure 2: Influence of zeta potential on particle-particle interaction.**

**Surface Morphology**
Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) provide a 3D image of the particle and morphology of surface along internal structure [56].

**Degree of Crystallinity**
Differential scanning calorimetry (DSC) was used to determine the thermal properties of drug and lipid excipients based on the crystalline phase with liposomes It is a thermoanalytical technique that was the quickest and most accurate method for determining the degree of crystallinity. XRD was one more technique that was frequently used to determine the blueprint of bulk lipids and physic mixture and evaluate the structure of solid lipid nanoparticles [39,55].

**Acoustic Methods**
This technique uses to determine the attenuation of sound waves that measure the size as well as surface charge. The energy was applied in nanoparticles while charge the particle saw the kinetic movement oscillating force was generated. The force defines the surface charge information [57,58].

**Scale up SLNs**
An apparatus design by Glasco and colleagues to formulate *SLNs*, that allow mild microemulsion to diffuse into cold water, resulting in massive amounts of SLNs being produced quickly [59]. The present device involves:
• Thermostatic aluminum chamber has worked piston as having to deliver micelles at such a designated fluctuation.

• There was a stainless-steel arch at the base of the aluminium chamber to the sterile membrane filter diameter (0.22 m), to lift the sterility of the merchandise.
• A Lure Lock connection connected the stainless-steel support to a needle. This device was housed in a jacket with an electrical thermostat. Production of SLNs by dissolving a good and comfortable microemulsion in an ice-cold cap containing water. Water was moved at a high and constant rate through a cylindrical magnetic bar (300 rpm).
• The microemulsion is dropped into the capsule by the needle. After the widespread microemulsion dripping, the SLNS diffusion was shaken for 15 minutes. The action point, such as the pressure tested to the gas cylinder, needle gauge, temperature of the aluminium chamber, and volume of dispersing water, primarily affect the particle size and PDI. The size of the resulting SLNs was the most. Furthermore, as the temperature at the needle increased, the diameter of the SLNS increased to about 26 nm, and a PDI of 0.1 was obtained 46. Gohla and Dingler standardized a method for producing drug-free and drug-loaded SLNs on a medium scale. High homogenization was used to produce batches weighing 3–15 kg. By combining two asynchronous homogenizers for 50 kg batches. To vary the SLN dispersion within the Lab 60 device as a second homogenizer, a Gaulin 5.5 device was used as the primary homogenizer. With 2–3 cycles of homogenization, 500 bar pressure was approaching the perfect pressure condition. The author's claim that SLN production would be easily high yield on an industrial scale [16,60].

**Drugs loading and Release facet SLNs**

Drugs loading within SLNs, with the help of nanocarriers for prolonged-release along with incentive active drugs release also lifted in research and reduce delivery of hydrophilic and toxic drugs. Drugs in SLNs by three main incorporation models [61,62].

Homogenous matrix model, incorporation of drugs in a form of amorphous also molecularly forms into the core. Application of hot and cold homogenization method incorporation into SLNs, the present model had frequently used for lipophilic drugs. Drugs enriched shell model drugs mark nearby the shell because yielding of drugs without lipid core. The drug's repartition within the resting lipid-lipid phase, the outer shell of the lipid core moderately increases the concentration of drugs. Drug-enriched core was only formulated for drugs liquefying into lipids due to drug saturation solubility through which nanoemulgel was made. Drugs melt in lipoid and precipitation of dugs since precipitation of lipid, during cooling drugs lead the precipitation of drugs also the lipid precipitation, just membrane towards incorporated drugs [63].

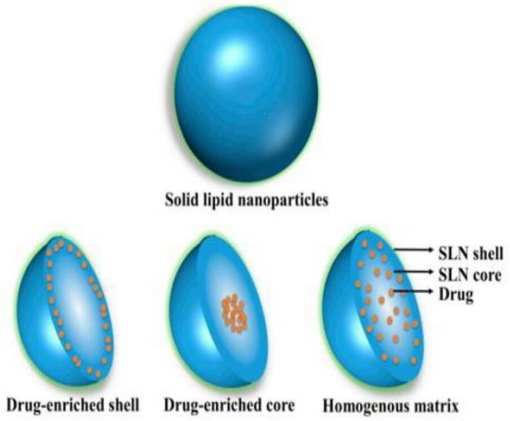


**Figure 3: Models of incorporation of active components into *SLN*.**

**Drug Release from SLNs**

The greatest importance of drugs release mechanism for each formulation. SLN release of drugs official through diffusion degradation and erosion. The mechanism of drugs release from matrix calculation lipids and its formation. Drugs were or ingrained into the matrix or on the outer surface in SLN, this scheme could show novel release prolonged release. SLN might show on the sport release effect because of drugs observed on the surface, it would be spread taken away of nanoparticle, after that origin can destroy depend on the lipid formation, the drugs release as a prolonged way. Solubility of drugs in water can control by the surface-active agent also temperature. Heat condition base drugs discharge halt bring burst discharge dugs out of SLN [64]. The assembly of SLN hold at room temperature because of burst discharge also filtration of drugs in water. Uncoupling of drugs in lipid phase while a control release absents of any instance discharge of drug will be observed through SLN. The basic idea of drugs discharge by SLN represent that the release was grieving by particle proportion. Small particle has increase drugs release as paralleled to the large particle. Then, drug release is completely reliant just on group of medications trapped in the SLN trap model, with drugs enriched shell model showing a high drug release. Venkateswarlu and Manjunath conducted in vitro release studies on clozapine-containing SLN. Clozapine was released using the Weibul and Higuchi equations rather than the primary order equation. Drug properties, such as solubility, may interfere with drug release parameters as well as the interaction with the lipid matrix (water or lipid soluble). Temperature affects drug solubilization in water because high enthalpy dissolves the drug, which can result in drug deposition on the outer surface of the lipid matrix [65]. External and internal cues have also been used to modulate drug release from SLNs. Based on the concept of a synapse, thermoresponsive SLNs have recently been described, based on the concept of a solid-liquid transition when heated A lipid mixture (lauric acid and monounsaturated fatty acid, dodecanoic acid, and linoleic acid) was used to create SLNs. At 39 degrees Celsius, the melting of the lipid core resulted in the rapid release of loaded 5-fluorouracil (>90 percent), whereas the solid core resulted in 22–34 percent drug release at 37 degrees Celsius [66]. Another study investigates cholesterol-PEG coated SLNs to see if they exhibit a PH-sensitive drug release pattern. These particles release loaded doxorubicin more quickly at pH 4.7 than at pH 6.8. The loss of electrostatic interactions between the charged lipid core dodecanoic acid (due to protonation) and the charged doxorubicin is thought to be the cause of accelerated release at low pH [67].

**Incorporated Bioactive Environmental Degradation Protection in SLNs**

SLNs involve bioactives within the core, avoiding drug interaction with environment to increase controlled release. As long as protection against proteolytic degradation is provided, SLNs significantly improve the acoustic properties of siRNA and peptides, and proteins, and should thereafter enable their prolonged release [83]. Acid labile medicines are protected from gastric acid destruction by SLNs, which operate as a cage. The antiprotozoal medication arteetherendoperoxide ring degrades in a gastric acidic environment, limiting its utility. Moreover, it must have been clearly established that by inserting it into SLNs, its decomposition could have been avoided, preserving the drug's function [84]. SLNs are already being used to stabilise as well as generate a DNA vaccine for dumdum fever [85].

**Route of administration for SLNs**

| Invasive | Mechanism | Characteristic | Reference |
|---|---|---|---|
| IV | The most researched route of administration for SLNs, particularly for Sport delivery, is intravenous (i.v.) injection. Yang et al. studied the pharmacokinetics of camptothecin into SLN after intravenous administration in mice. When compared to a simple drug solution, SLNs improve bioavailability and mean residence times (MRT), particularly in the brain. The accretion of SLN in the nervous system, as opposed to other organs, suggests that this carrier has a brain targeting potential. | Hydrophilic | 68 |
| IM | Patient reduces pain along with reducing discharge time by post laparoscopic surgery. Hence novel class of drugs was used, like NSAID also opioids. The main purpose to compare the analgesic and opioids spring efficacy diclofenac (IM) with diclofenac patches administration of post laparoscopic pain. in both groups were higher potential into 4 h, There were no significant differences between both groups. Tramadol to reduces analgesic and IM injection pain was observed, both the group there was no skin irritation was noticed during the application of a specific site | Lipophilic and hydrophilic | 69 |
| Non- invasive | | | |
| Oral | Oral route extremely painless route for delivering SLNs, and administered in the form of a suspension or a solid dosage form Mangesh Bhalekar et al. created darunavir-loaded SLNs to increase the drug's bioavailability. The hot-homogenization technique was used to create darunavir-loaded SLNs. Darunavir oral bioavailability was significantly increased due to the high intestinal lymphatic uptake of drug-SLNs. | Lipophilic | 70,71,72,73 |
| Pulmonary | The pulmonary route can deliver drugs in an exceedingly spread specifically with the assistance of Any equipment or inhaler to attain circulation, bypassing the first-pass metabolism, or to treat diseases affecting the fewlung. For the treatment of lung diseases, lipid nanocarrier techniques are used to increase drug absorption and transport efficacy into alveolar macrophages. | Hydrophilic | 74 |
| Topical | SLNs formulation was used for topical application because of its biocompatible nature. In comparison to the free drug, a lipophilic drug was loaded into visible SLNs for greater skin penetration. SLNS was a sustained release in nature. Such polymer was controlled by the addition of excipient, suddenly controlled release of drugs was observed. | Lipophilic | 75,76,77,78 |
| Ocular | Ocular delivery had been shown as a better permeability of SLNs. In ocular mucosa, the drugs could be prolonged release, which analyzed the current ophthalmic solutions because of sustained retention time by the drugs. SLNS in nanosize does not interfere with vision. After all, in SLNS during the formulation of ocular delivery must have the unique parameter that was (Draize rabbit eye test), sterility, isotonicity, and ph (almost identical to lachrymal fluid). The use of high-pressure homogenization in the formulation of SLNs resulted in the prolonged delivery of active from the in-gelling structure. | Hydrophilic& Lipophilic | 79,80,81,82 |

**SLN surface engineering**

Surface engineering improves SLN bioactivity and targetability. To overcome drug resistance and extend anticancer activity, Wang et al. developed a hyaluronic acid (HA) embellished, Pluronic 85 (P85) coated, paclitaxel (PTX) stocked SLN (HA-PTXP85-SLN). Heat homogenization yielded SLNs with a mean size of 160 nm and a PTX collected specifically of 4.9 percent. In comparison to free PTX, SLN loaded with PTX showed prolonged drug release. According to the findings, HA-modified SLN accelerated tumour accumulation and thus slowed the growth of PTX-resistant tutors significantly [86]. Baek et al. recently modified its area of a SLN by coating it with N-carboxymethyl chitosan (NCC) to improve curcumin bioavailability. The coating's goal was to prevent curcumin degradation by lowering the burst release of curcumin from SLN in an acidic stomach atmosphere. In-vitro release experiments revealed that NCC coated SLN release a small quantity of medication in stomach fluid, whereas unmodified SLN release in bursts. In simulated intestinal fluid, however, persistent release was seen, indicating that the coating was effective in delivering the majority of the medication to the intestine. Furthermore, NCC modified SLN had a higher area under curve (AUC) and Cmax of curcumin in vivo. These findings demonstrate that NCC modified SLN improves intestinal absorption by increasing lymphatic uptake (allowing formulations to avoid CYP3A-mediated hepatic first pass metabolism) and decreasing medication breakdown in an acidic condition [87]. Wang et al. developed a chitosan-coated, cisplatin-loaded SLN (CChSLN) with enhanced anticancer properties throughout cervical cancer. When compared to uncoated particles, CChSLN showed better effectiveness in killing cancer cells in an in vitro cytotoxicity assay. The higher apoptotic potential of CChSLN compared to uncoated SLN and free drug may explain the improved internalisation (due to cationic charge) and controlled release of medication obtained from CChSLN formulation [88].

**Applications of SLNS**

Increase the bioavailability of SLNS through the entrapment of drugs by conversion of disintegration rate, while advanced tissue allocation also allows for drug targeting the following table summarizes the SLNS operations as reported in the literature. More patented SLN-based delivery systems are expected in the near future.


**Figure 4: SLN applications are depicted schematically.**

**Application of SLNs in TDDS**

| Application | Drugs loaded in form of SLNs in transdermal patches | Target site /Target site | Activity | Reference |
|---|---|---|---|---|
| Non- steroidal anti-inflammatory agent (NSAID) | Piroxicam | Cyclooxygenase inhibitor | • To improve the permeation and to enhance the bioavailability | 22 |
| Anti-diabetic | Metformin | Inhibit hepatic gluconeogenesis | • Increase the bioavailability of drugs directly into the blood stream | 23 |
| Type-2 Diabetic | Repaglininide | Stimulates beta cells in pancreatic islets and lowers blood glucose level | • Increase the infiltration of drugs<br>• Extend the release of drugs<br>• Decrease the dose frequency | 24 |
| Anti-diabetic | Sitagliptin | DPP-4 inhibitor | • Increase and prolonged actions | 25 |
| Anti-hyperlipidemic | Simvastatin | Competitively inhibiting HMG- CoA reductase | • To increase the bioavailability of drugs | 26 |
| Anti-hypertensive | Ramipril | ACE inhibitor | • To improve the systemic bioavailability of Ramipril | 27 |
| Antioxidant | Vitamin A | Function in the retina | • To improve the penetration of vit-A | 28 |
| Corticosteroids | Betamethasone dipropionate | Immunosuppressor | • To enhance the permeation and to improve bioavailability of drugs | 29 |
| PDEF5i | Avanafil | PDEF5 inhibitor | • To hold the rate of drugs<br>• Increase the infiltration of drugs. | 30 |
| Natural product solitary from the Chinese plant tripterygiumwilfordii hook F | Triptolide | Inhibits expression for the p40 gene. | • To enhance the bioavailability of drugs | 31 |
| Non-steroidal anti-inflammatory | Flubiprofen | COX-1, COX-2 inhibitor | • To the hance the bioavailability of drugs and to enhance the permeability | 32 |
| Anti-Alzheimer drugs | Rivastigmine | Preventing the hydrolysis of acetylcholine, and thus leading to an Increase concentration of acetylcholine at cholinergic synapses | • Site specific and control drugs release.<br>• Protection of drugs against chemical degradation<br>• High drugs pay loading<br>• Ease of manufacturing | 33 |
| Hormones | Testosterone | Activation of the androgen receptor directly or as DHT and by conversation to estradiol and activation of certain estrogen receptors. | • Protection of drug against chemical degradation<br>• High drugs pay loading<br>• Ease of manufacturing | 34 |
| NSAID | Etoricoxib | COX-2 selection Inhibitor | • Spike the percentage of drugs locally<br>• prolong time<br>• Lower the risk of unsystematic toxicity | 35 |
| Anti-inflammatory | Curcumin | Inhibitor of cell signaling pathway | • Prolong the effect of drugs<br>• Prolong the existence ofdrugslocally | |
| Glucocorticoid or corticosteroids | Mometasone | Corticosteroid hormones receptor Agonist | • To increase the penetration of drugs | 36 |
| First generation antihistamine | Promethazine theoclate | Histamine H-1 blocker | • To improve the therapeutic efficacy | 37 |
| Antifungal drugs | Amphotericin B, Nystatin and ketoconazole | Inhibit the synthesis of ergosterol(the main fungal drugs) | • To reduces side effect<br>• To maximize the antifungal drugs activity | 38 |
| Anticancer drugs | Cytarabine | Prohibit the fusion of DNA specific for the S phase of the cell cycle | • To sustain release<br>• To improve therapeutic activity | 39 |
| Topical retinoid | Tazarotene | Retinoic acid receptor specific retinoid | • To improve the skin tolerability<br>• To improve patient acceptance and topical delivery of tazarotene | 40 |
| Terpenoid | Neem | Anti-inflammatory | • To improve therapeutic activity | 41 |

**Controlled released of drugs**

SLNs promote the release of loaded drugs either by the changing of surface properties or by varying loading approaches. During a recent study, TNF- siRNA loaded SLN had been investigated to evaluate the prolonged effect in the treatment of auto-immune disease. The solvent displacement method was used to create SLNs from biocompatible lecithin and cholesterol. An in-vitro release study with siRNA reveals that there is no burst release and that only about 5% of the siRNA is released in 30 days. Due to the presence of cholesterol, the extended-release property of the formulation to have existed. Cavalil et al. used Cyclodextrin to co-precipitate inclusion complexes containing hydrocortisone and progesterone [89]. It was observed that the drug-cyclodextrin complex delayed the release of drugs from SLNs [90]. This was challenging to achieve controlled release due to the poor loading of the drug in the formulation. Controlled release of gonadorelin was achieved using SLNs due to their high pliability to load a high amount of drug up to 69.4 percent besides solvent diffusion method. After the enhance of burst, (Approximately 24.4 percent during the first 6 hours) A prolonged drug release pattern of about 12 days was observed, as well as an anti-acne SLN-based gels for topical drug delivery of adapalene for acne treatment was

developed [91]. Kim et al. created a new formulation to help the pH-sensitive mechanism [92]. Curcumin, that acts mostly as depot in this system, was coated with a mesoporous silica matrix to monitor curcumin release. This complex typified a PH-dependent drug release pattern, which could be responsible for communication among silanols on the mesopore top layer as well as curcumin [93].

**Targeted Brain Drug Delivery Using SLNs**

By increasing the drug's flexibility, SLNs can aid in its passage through the barrier (BBB). Abbas et al. used nanolipid carriers co-loaded with superparamagnetic iron oxide nanoparticles (SPIONs) for both nanocarrier guiding and holding in an external force field to deliver clonazepam to the brain via intranasal olfactory mucosa. Because the nano-lipid carriers are embedded in thermosensitive mucoadhesive gels, clonazepam administration is improved. This study sheds light on a new intranasal epilepsy treatment that reduces the peripheral side effects of clonazepam [94].

**Anticancer Drug Delivery via SLNs**

Anticancer drug delivery using SLNs has recently been explored for carcinoma treatment, with findings indicating a sustained release of tamoxifen with a favourable therapeutic effect [95]. With the use of an acceptable targeting ligand, surface modified SLNs can be made for tumour targeting and Anticancer medications such as methotrexate (MTX) or even camptothecin are delivered effectively [96]. Gomes et al. developed lipid core nanoparticles (LDE) that contained the chemopreventive drug PTX and observed that cholesterol feeding reduced atherosclerotic lesions in rabbits. In comparison to the LDE-single group, the LDE-PTX and LDE-PTX+LDE-MTX managements can grow whilst also 50 and 61 percent enamel area regression, respectively, after stopping cholesterol feeding. The LDE-PTX and LDE-PTX+LDE-MTX tumour necrosis organic phenomenon factor was reduced by 65 and 79 percent, respectively. This research demonstrated the effectiveness of combination chemotherapy in treating highly atherosclerotic inflammatory lesions [97]. Chorio et al. created a distearoyl-floxuridine-loaded SLN with an entrapment ability of 70.8–82.8 percent. Human neoplastic cell types such as HT-29, MDA-MB231 but also M14 were studied in vitro for cytotoxicity revealed that distearoyl-floxuridine SLN had superior neoplastic cell killing activity. Distearoylfloxuridine SLNs were found to be 100 times more efficient than free floxiredene. Furthermore, clonogenic assays revealed that distearoyl-floxuridine SLN has higher cytotoxicity than free drug [98].

**Antibiotic Drug Delivery Using SLNs**

SLNs deliver antimicrobial payloads to lymphatic locations, allowing infectious bacteria to be effectively eliminated [16]. Nanoparticles, as well as nanostructured surfaces, inhibit the spread of germs and diseases, which is a good solution for biofilm and antibiotic resistance problems. SLNs are antimicrobial drug delivery systems that work against bacteria by encapsulating antimicrobial medicines, disrupting microbial adhesion, and attaching to cellular surfaces via receptors [99].

**Gene Carrier SLNs**

SLNs containing genetic materials like plasmid deoxyribonucleic acid (p-DNA), DNA, and some other nucleic acids have been the subject of several investigations [97]. SLN-based vectors, according to Vicente-Pascual et al, could be a useful approach for genetic modification in the treatment of corneal disorders and inflammation [100].

**Topical SLNs**

Axerophthol, isotretinoin, and flurbiprofen are among the medications delivered via topical SLNs. Flurbiprofen-loaded SLN gel can be administered to a target site to increase drug tissue concentrations in a controlled manner [53].A non-steroidal medication called SLN loaded diflunisal (DIF) has also been developed for the treatment of arthritis. The warm homogeneity method (depending on microemulsification method) yielded globular SLNs with an average diameter of 123.0 2.07 nm (PDI 0.295 0.16) and a mean size of 123.0 2.07 nm (PDI 0.295 0.16). (PDI 0.295 0.16). These SLNs significantly reduced fluid volume, granuloma tissue weight, and leukocyte count/mm3 in a mouse air pouch model. Using SLN formulation resulted in 2.30 and 1.29 times increase in inhibition efficiency of oedema, respectively, in a mouse ear oedema model and a rat paw oedema model, when compared to the standard cream [101].

**Cosmetics SLN**

S SLNs are innovative nanocarriers that will replace traditional delivery systems in cosmetics such as creams, gels, and ointments [58,102]. Curcumin (CUR) has therapeutic potential against skin problems, according to Gonçalez et al (SD). Non-anionic SLNs (CSLN) containing CUR had all been developed and physiochemically investigated besides SD. CSLN surface charge (zeta potential, +23.1 to +30.1 mV) was implicated in the development in medication preferential accumulation to sick tissue [103]. On the basis of occlusiveness, Jose and Netto especially in comparison lipid nano-based mechanisms to conventional cosmetics. In contrast to a typical glycerine item, the corresponding input on surface utilising lipid nanoparticles has been seamless. UV-blocking and photoprotection activity of SLN-based products was impressive [58].

**SLNs as a Vaccine Adjuvant**

Immunologic adjuvants are substances that are being used to boost the level of activation, stimulation, and reliability of vaccines. During a certain time, Stelzner et al. created a squalene-based adjunctive model for a yeast-based vaccine using steam-sterile SLNs. The size of squalene-loaded SLN was reported to be between 120 and 170 nm using static and DLS techniques. The proposed vaccination adjuvant exhibited great efficacy against the dangerous bursal virus illness in a mouse model. Squalene-based adjuvants displayed great biocompatibility as well as immune stimulating qualities, similar to Freund's adjuvant [104].

**SLNs in Antitubercular Chemotherapy**

SLNs as well as other nanocapsules are currently has been used to exterminate Mycobacterium tuberculosis completely [105]. An oxidative model throughout airway epithelial cells was used, according to Castellani et al., SLNs might be an efficient drug delivery route besides natural anti-oxidants derived from grape seed. Inside cells, long-term persistence and stability, as well as proanthocyanidin liberation, were highlighted by the authors. Their findings pave the way for new anti-inflammatory and anti-oxidant treatments for chronic respiratory illnesses [106].

**SLNs in Bio imaging**

To ensure safe administration and avoid septic shock, it was critical to identify and remove lipopolysaccharides (LPS) from pharmaceutical formulations but also food. The goal of an abiotic system based on SLNs is to capture, detect, and remove LPS in aqueous solutions in a reversible manner. Furthermore, the regenerated particles serve as colorimetric markers in dot blot bioassays for basic and rapid measurement of LPS removal [107]. In the advanced field of nanomedicine, there are several options for rheumatoid arthritis (RA) therapy. Albuquerque et al. developed an anti-CD64 antibody-anchored SLN-based thermostatic model comprising SPIONs and MTX (co-encapsulated in the SLNs) to

target macrophages in RA patients. Each preparation is less than 250 nm in size and have a -16-mV zeta potential, making them suitable for IV injection. SPIONs were encased within the SLN matrix, as seen by transmission electron microscopy (TEM) images, and MTX association efficiency was better than 98 percent. In vitro tests on THP-1 cells revealed that all formulations were cytotoxic at low concentrations up to 500 g/mL. As a result, SLN-based preparations have the potential to be used in respectively medicinal and application development [108].

**Aspects of SLN Toxicity**

Components for use in drug delivery applications should be biocompatible, as well as biocompatibility testing was a critical consideration. While in vivo investigations are required for a precise assurance of a formulation's toxicity, a variety of in vitro toxicological experiments done in appropriately selected cell lines can provide incredibly useful information. Such approaches are typically regarded one of the first to detect toxicity [109].

**SLN cytotoxicity**

The indication with viable cells or toxic effects continues to remain the much more widely used parameter to validate biocompatibility or toxicity. The cytotoxicity of SLN made with glyceryl monostearate has been investigated. Acute lymphoblastic cells and monkey kidney epithelial cells (VERO) were tested in vitro. MTT assay on leukemic cells (L1210) The assertoric (IC50) of SLN was determined to just be 0.7 and 0.4 mg/mL in Pseudomonas aeruginosa cell but also 0.5 and 0.3 mg/mL in L1210 cells after 24 and 48 hours of incubation, respectively [110]. Another study looked at the toxicity of SLNs made with MCF-7 and MDA-MB231 cells were homogenised with Softisan 154 and soy lecithin using an elevated homogenization process. The IC50 values for MCF-7 cells after 24, 48, and 72 hours were found to be around 0.28, 0.26, and 0.23 mg/mL, respectively. Similarly, the IC50 values for MDAMB-231 cells after 24, 48, and 72 hours were 0.29, 0.29, and 0.27 mg/mL, respectively [111]. It has been demonstrated that the lipid used to create nanoparticles has a significant impact just on cytotoxic activity of a resulting SLNs.

**The Effect of Surface Charge**

The surface charge of the particles determines the impact of charge density on colloidal nanoparticles and cells. Non-ionic surfactants being used SLNs could still cause membrane integrity to be distorted [112], making the process more sensitive100.

**Compositional Effects on Cell Viability**

The detection of such surfactants for use in SLNs was critical for the SLNs system, not just for biocompatibility but for consistency and lifespan. Pluronic F-68 and Tween 80 topical, oral liquid, and semisolid dose formulations were used. All these surfactants (Pluronic F-68 and Tween 80) found in SLNs were tested for viable cells. Pluronic F-68 in SLNs demonstrated better stability as well as cell viability of 90%, so while Tween 80 in the same lipid content demonstrated superior stability but only 50% cell viability [113]. This same type of emulsifier used in SLNs, as well as the length of time SLNs are in contact with cells, will affect cell viability [114].

**Genotoxicity**

NA was evaluated by gel electrophoresis [115,116]. However, a study found that acetyl shikonin-bearing SLN caused DNA damage, as a result, comet formation in A549 cells increased. Whenever the medication had been enclosed in SLN, the DNA damage increased even more [117].

**Haemolytic Toxicity**

Hemolysis tests were used to assess the extent of erythrocyte destruction caused by an intravenous injection of a foreign substance [118]. Lakkadwala et al. investigated the hemotoxicity in SLNs made up of glycerol monostearate and polysorbate 80, and found that even at high doses (1 mg/mL), SLNs had low hemotoxicity. Regardless of whether the formulation had a cationic or anionic surface, hyaluronic acid-coated SLNs containing antineoplastic drugs had low haemolytic toxicity [119]. A further doxorubicin-containing non-hemolytic cationic SLN was discovered. While SLNs had been covered, the impact was articulated as well. This effect was also observed when galactose-coated SLNs were used [120].

**Formulations of Solid Lipid Nanoparticles on the Market**

To improve the bioavailability of BCS class II medicines, lipid-based formulations are used. Oral lipid-based formulations account for approximately 4% of commercially available products in the United States, the United Kingdom, and Japan. Simple lipid solutions to self-emulsifying drug delivery (SEDDS) systems are examples of oral lipid-based systems [121].

## CONCLUSION

The search for novel transdermal patches containing SLNs with unidirectional delivery of drugs is currently in progress to overcome the low permeability, deterioration by gastrointestinal enzymes, abnormal absorption, fluctuation in drug plasma level, drug degradation first-pass metabolism of a wide range of pharmacological drugs. To combat these issues, SLNs in transdermal patches are one of the most appropriate and conventional dosage forms because they are easy to use and increase patient compliance. A wide range of polymers is being used to achieve satisfactory results in patch formulation, which is difficult to achieve with traditional dosage forms. SLNTP benefits include not only avoiding the first-pass metabolism but also improving drug permeation through the skin, which directly acts on this site of action.

**Future Perspectives**

This review is a small effort to summarize the work done and to show the future aspects of preparing transdermal patches with natural polymers. However, the need for safe and effective transdermal permeation/absorption enhancers is critical for a promising future in transdermal drug delivery.

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