WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 2, 203-211. Review Article ISSN 2277–7105

REVIEW ON TRANSDERMAL PATCH

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Article Received on
21 November 2024,

Revised on 11 Dec. 2024,
Published on 15 Jan. 2025

DOI: 10.20959/wjpr20252-35202

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Review on transdermal patch

The transdermal drug delivery route has significant advantages over the conventional oral route. It can provide more patient compliance, especially in patients with swallowing problems, more stable serum drug levels, pain-free drug administration, avoiding hepatic first pass metabolism and drug degradation in the GIT, food-drug interaction and reducing side effects. TDDS is suitable for long term administration, especially for insulin and analgesic drugs. However, the low skin permeability which limits drug penetration and inconsequence affects drug bioavailability, represents the most challenging mission for delivering. Nanostructured lipid carrier (NLC) is the second generation of lipid nanoparticles, which was created to overcome the drawbacks of the solid-lipid nanoparticles (SLNs), such as the low drug loading capacity, gelatin and reduced stability. Transdermal drug administration is a successful method of increasing drug bioavailability. The transdermal route is a potential alternate route with a variety of characteristics that might be advantageous. The location and adherence of the patch at the site of action, the lipid solubility of the drug molecule and the structural contents of the lipids and proteins in the epidermis are modifying variables that influence transdermal absorption as well as drug bioavailability. The lipid nanoparticle-based method by transdermal delivery is regarded as a safe choice due to improved patient compliance and controlled release relative to other delivery systems. The NLCs consist of combination of liquid and solid lipids, leading to a lower melting point for solid lipids while remaining solid at body and room temperature. Lipid nanoparticles have a variety of features that make them suitable for topical usage in cosmetics and medicinal formulations. Because of extensive positive benefits such as skin hydration, skin occlusion and skin targeting, NLCs have a significant potential in the pharmaceutical market. Skin hydration is important for API topical distribution because it

hydrates the skin, which causes the pores to open. Nanoparticles are colloidal particles that range in size from 10 to 1000nm. Surface modification of NLCs is also possible. Nanotechnology has revolutionized the field of drug delivery systems, offering improved efficacy, stability, and bioavailability of therapeutic agents. This review highlights the application of nanotechnology in the treatment of hypertension, a major risk factor for cardiovascular disease.

The application of nanotechnology in drug delivery systems has transformed the treatment of various diseases, including hypertension. Building on the success of nanostructured drug delivery systems in improving the efficacy of therapeutic agents, researchers have explored the potential of nanocarriers in transdermal delivery of antihypertensive drugs. Hypertension, a major risk factor for cardiovascular disease, affects approximately one-third of the adult population worldwide. Antihypertensive drugs like metoprolol, atenolol, and amlodipine are commonly used to treat hypertension, but their oral delivery is associated with side effects, low bioavailability, and poor patient compliance. Transdermal delivery offers a promising alternative, providing a non-invasive and convenient route for drug administration. NLCs have been explored as a potential transdermal delivery system for antihypertensive drugs, offering improved drug solubility, stability, and bioavailability. By leveraging the benefits of nanotechnology, researchers aim to develop more effective and patient-friendly treatments for hypertension, ultimately reducing the burden of cardiovascular disease.

Similarly, the treatment of hypertension also faces challenges with conventional drug delivery systems, such as poor bioavailability, low solubility, and rapid metabolism. To overcome these limitations, nanocarrier-assembled nanosized drug delivery systems have been explored as a promising approach for antihypertensive drugs.

Types of nanostructured lipid carriers are

1. **Imperfect type:** The liquid phase lipid content of the Imperfect kind of NLC is quite low. It is made up of saturated and unsaturated lipids with varying fatty acid chain lengths, which causes flaws in the lipid matrix and drug storage compartments.

2. **Amorphous type:** The amorphous version of NLC produces a solid lipid with no crystalline structure. This type of NLC is made by combining solid and liquid lipids, such as hydroxyoctacosanyl hydroxystearate isopropyl myristate.

3. **Multiple type:** Oil nano compartments are coated with solid lipid and medication is dissolved in the oil compartment in several types of NLC.

Rational Use of Nanostructured lipid carrier for transdermal delivery of metabolic disorder

1. NLC enhances the drug delivery through increased skin permeation due to its smaller size.
2. Due to occlusive nature of small particle size increase hydration in the skin layer and elasticity which result in better permeation because of less water evaporation from the skin surface.
3. Increase in surface area to volume ratio: Atoms and molecules at surface or interface have different environment and bonding configuration and thus these exhibit different characteristics.
4. Quantum Size Effect: When the size of the particle is comparable to phase coherent length of electrons, the energy spectrum is quantized into discrete levels.
5. Nanotechnology in hypertension treatment has shown potential in improving drug solubility, stability, and bioavailability, leading to enhanced therapeutic efficacy and reduced side effects.
6. Nanostructured lipid carriers (NLCs) have emerged as a versatile and efficient nanocarrier system for transdermal delivery of antihypertensive drugs, offering improved drug penetration, sustained release, and targeted delivery.
7. By leveraging the benefits of nanotechnology, researchers aim to develop more effective and patient-friendly treatments for hypertension, ultimately reducing the burden of cardiovascular disease. This review highlights the potential of nano formulations in addressing the challenges of antihypertensive drug delivery and achieving better therapeutic outcomes.
8. Lattice contraction: At very small sizes of the order of a few nm, lattice parameters may reduce because of inward inter-atomic forces. Structural phase change, such as from cubic to hexagonal, has also been observed in this size range.

MATERIAL AND METHOD

High-Energy method

This method involves hot and cold high-pressure homogenization tactics to develop NLCs. Another method that falls under this category is the high-shear/high-speed homogenization method.

(1) Hot High-Pressure homogenization method

Here, solid lipids are melted by heating usually 5–10°C above the melting temperature, and then, liquid lipids are added along with the drug(s), followed by adding this dispersion to a hot surfactant solution in water. The mixture is then homogenized using high pressure (100–2000 bar), leading to the formation of a hot oil in water primary emulsion, which after cooling (liquid nitrogen or dry ice) settles into a form (NLCs). Elevated temperatures help in reducing the particle size as the viscidness of lipids gradually drops. To obtain a narrow particle size distribution, the emulsion is usually subjected to ultra-sonication.

(2) Cold High-Pressure homogenization method

The cold high-pressure homogenization method involves the melting of solid/liquid lipids/drug(s) and solidification by liquid nitrogen or dry ice. The mixture is then milled and assorted to a cold surfactant solution, resulting in the formation of a presuspension, which is then subjected to high-pressure homogenization (5–10 cycles, 1500 bar pressure), leading to the formation of NLCs. Both these methods offer advantages such as the use of minimal toxic solvents, easy scale-up technique, and quick NLC formulation.

(3) High Shear/High-Pressure homogenization method

Solid and liquid lipids are melted 5–10°C higher than their melting points and then mixed with the drug. To this, simultaneously heated to an equivalent temperature, a surfactant solution is added. This mixture is then homogenized at a higher shear pressure to yield low-particle-sized hot oil in water Nano emulsion, which after cooling and ultra-sonication settles into a homogeneous NLC formulation.

(4) Melt Emulsification homogenization method

This method involves dispersing solid and liquid lipids along with the drug into an aqueous surfactant solution, which is then subjected to probe sonication. Later, the blend is cooled to obtain NLCs.

Low-Energy method

(1) Microemulsion method

This method involves a simpler method to fabricate NLCs in which the molten lipid is blended into the mild hot liquid lipid along with the addition of medication. Then, under constant stirring, the aqueous emulsifier solution and lipid blend are added to the melted lipid mix, leading to the formulation of microemulsion. The microemulsion is disseminated instantly in ice-cold water (0–4°C) around 20–50 times the volume of the microemulsion, which leads to the precipitation of microemulsion globules, creating NLCs. Ice-cold water supports the formation of smaller particles without aggregation and homogeneous preparation. High-volume water may lead to dilution, which may be countered by lyophilisation. Although the method is simple, it requires a high volume of emulsifiers and coemulsifiers.

(2) Double emulsion method

The aqueous phase containing the hydrophilic drug is dispersed into the organic phase (melted solid lipid and liquid lipid) forming primary water in oil emulsion. This primary emulsion is again dispersed into the aqueous phase, forming a w/o/w double emulsion in which the hydrophilic drug is enclosed in the inner watery continuous phase. This method involves a solvent evaporation method but generates large particle-sized nanoparticles.

(3) Membrane contractor method

In this method, the melted lipid is pressed through the pores of the membrane at a pressure that leaves the temperature of the system higher than the melting points of the lipids used. The lipid globules coming out of the pores are distributed away by the aqueous surfactant under turbulence, flowing just below the membrane. Upon cooling at room temperature, NLCs are formed. The process is complex and involves the use of sophisticated instruments, and particle size depends on the rate of flow of the watery phase, its temperature, lipid phase pressure, and membrane pore size that may be susceptible to blockage.

(4) Phase inversion method

The phase inversion method involves two-step processes, where the first step involves formulation of w/o emulsions by integrating lipids, water, and emulsifiers at elevated temperatures (up to 85°C). Then, phase inversion is attained (from w/o to o/w emulsion) by sudden cooling of the emulsion with constant stirring followed by a further drop in temperature by adding cold water (0°C). This causes the transition of minute lipid droplets to

recrystallize into Nano lipid carriers. The stability of such a system relies on the regulation of the temperature cycle. This method produces particles below 50 nm but involves a high ratio of emulsifiers. In addition, this method is cost effective and is devoid of toxic solvent involvement.

(5) Coacervation method

This method allows thermosensitive lipids to be developed as NLCs without the use of toxic solvents. Here, an amphiphilic emulsifier is added to the lipidic blend in an acidic environment (coacervation solution) to form NLCs.

Organic solvent employed method

(1) Solvent evaporation emulsification method

This method involves the use of water-immiscible organic solvents, such as example dimethyl sulfoxide (DMSO), chloroform, cyclohexane, and dichloromethane (DCM), in which drugs and lipids are dissolved. The blend is then stirred in an emulsifying aqueous phase and further sonicated or homogenized to obtain a homogeneous NLC formulation with uniform particle size and size distribution. The use of an organic solvent is an obvious disadvantage.

(2) Solvent diffusion emulsification method

Water-mixable organic solvents are employed, for example, methanol, ethanol, acetone, benzyl alcohol, and ethyl formate, to dissolve the lipids and drug. The process involves sonication of the mixture at an elevated temperature to create a distinct lipid phase. Subsequently, this lipid phase is blended with an aqueous surfactant solution, which is also maintained at a similar temperature as the lipid phase, with continuous stirring. Dispersion was stirred at room temperature to cool off and evaporate the organic solvent to obtain nanosized lipid carriers.

(3) Solvent injection method

The method is quite similar to the solvent diffusion method where water-miscible organic solvents are used. The difference is that lipid is injected into the aqueous surfactant solution, and the globules are injected out of the needle. The surfactant solution was kept under turbulence using a stirrer to aid in the quick solubilization of the lipid. The emulsion so formed is filtered to eradicate superfluous fat. The selection of solvent and surfactant concentrations impacts the size and size distribution proportionately. The method itself is

unique as it allows the formulator to use simple techniques without the use of sophisticated instruments.

(4) Supercritical fluid method

The medication and lipids are solubilized in an organic solvent with the emulsifier, leading to the formation of an organic solution. This is then dispersed into the watery phase, followed by high-pressure homogenization, which creates an oil-in-water emulsion. Lipid nanoparticles are formulated by injecting the o/w emulsion from the top of an extraction column while simultaneously introducing a supercritical fluid, typically carbon dioxide, at a constant flow rate to ensure complete solvent removal.

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