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Review on Transdermal Drug Delivery System

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Abstract

To get beyond the challenges of drug delivery, particularly oral route, transdermal drug delivery method was introduced. A transdermal patch is a medicated adhesive patch applied to the skin in order to transdermally administer a particular dosage of medication into the bloodstream. It encourages healing of a body part that has been wounded. A transdermal patch offers a controlled release of the medication into the patient, typically through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. This is an advantage of transdermal drug delivery over other types of delivery systems such as oral, topical, i.v., i.m., etc. The skin is a very effective barrier, thus only drugs whose molecules are tiny enough to permeate the skin can be administered in this way. This is the fundamental drawback of transdermal administration systems. The preparation processes for several transdermal patch types, including matrix patches, reservoir type, membrane matrix, drug-in-adhesive patches, and tiny reservoir patches, are covered in this review article. Also, the various transdermal dosage form evaluation techniques have been reviewed.

Keywords: Transdermal Patch, Reservoir System, Matrix System, Micro Reservoir System, Polymer Matrix, Evaluation, Future.

Introduction

The rate at which the liquid medicine contained in the reservoir within the patch can flow through the skin and into the bloodstream is controlled by a specific membrane in transdermal patches (also known as skin patches).

For use in a skin patch, some medications need to be mixed with chemicals like alcohol that boost their capacity to permeate the skin. Skin patches can be used to deliver medications such as scopolamine (for motion sickness), nicotine (for quitting smoking), oestrogen (for menopause and to prevent osteoporosis after menopause), nitroglycerin (for angina), and lidocaine (for shingles pain) (herpes zoster). Yet, many chemicals, including insulin molecules, are too big to penetrate through the epidermis.

Patches that are placed to the skin take the place of syringe or pump-based vascular access. The first transdermal patch for the treatment of motion sickness received FDA approval in 1979 after being developed in the 1970s. The patch that supplied the scopolamine lasted for three days. Nitroglycerin patches were legalized in 1981, and today there are patches for many different medications, including clonidine, fentanyl, lidocaine, nicotine, nitroglycerin, oestradiol, oxybutynin, scopolamine, and testosterone.

Together with hormone replacement, there are combination contraceptive patches available. The duration of the patches typically ranges from one to seven days, depending on the medication. [1]

Topical remedies anointed, bandaged, rubbed or applied to the skin are likely to have been used since the origin of man, with the practices becoming evident with the appearance of written records, such as on the clay tablets used by the Sumerians.[2]

Definition

A transdermal patch, also known as a skin patch, is an adhesive patch that is applied to the skin and contains medication that is intended to be absorbed through the skin and into the bloodstream.

Advantages

- Topical patches offer a painless, non-invasive method of delivering medications right into the body
- Topical patches are a superior delivery method for medications that are extensively destroyed by the liver, poorly absorbed from the gut, or broken down by the stomach's acids.
- Topical patches used in conjunction with a slow, controlled release of medication over an extended period of time.
- Compared to oral drugs or supplements, topical patches have fewer negative effects.
- Topical patches are less complicated to use and to keep in mind.
- For those who cannot or do not want to take drugs or supplements orally, topical patches provide an alternative.
- The use of topical patches is economical.
- Topical patches are more popular.

Disadvantages

- Ionic medicines cannot be delivered via TDDS.
- TDDS is unable to achieve high drug concentrations in the blood or plasma.
- It is not possible for medications with huge molecular sizes to develop.
- Pulsatile drug delivery is not possible with TDDS.
- TDDS cannot occur if the medication or formulation irritates the skin.[3]

Transdermal Drug Delivery Systems Types

Drug-in-Adhesive System with One Layer

The medicine is included in the adhesive layer of this sort of patch. In addition to holding the numerous layers together and attaching the entire device to the skin, the adhesive layer also releases the medicine.

Reservoir system

With this system, a backing layer and a membrane that regulates flow rate sandwich a drug reservoir. Also regulated medication release by micro porous materials membrane. The drug may be disseminated in a solid polymer matrix, a solution, suspension, gel, or the reservoir compartment.

Matrix system

a)Drug-in-Adhesive System: The drug is disseminated in an adhesive polymer to create a drug reservoir.Then applying the medicated polymer glue by solvent casting or, in the case of hot-melt adhesives, by melting the adhesive to a layer of impervious backing.

b) The matrix-dispersion system, in which the medication is uniformly distributed within a hydrophilic or lipophilic polymer matrix. And in a compartment made from a drug-impermeable backing layer, this containing

polymer and drug are attached onto an occlusive base plate. With this approach, the adhesive is applied around the perimeter rather than directly to the face of the drug reservoir to create an adhesive rim.

Micro reservoir system

This system combines matrix-dispersion and reservoir systems. In this method, the drug is suspended in an aqueous solution of a water-soluble polymer before being uniformly dispersed in a lipophilic polymer to create thousands of unleachable, microscopic drug reservoir spheres.

Polymer matrix

The transdermal drug delivery method is built on polymers. Systems for transdermal delivery are made of multilayered polymeric laminates, which have two polymeric layers that serve as an adhesive and/or rate-controlling membrane and a drug reservoir or drug-polymer matrix sandwiched between them. The outer impervious backing layer prevents the loss of the drug through the backing surface.

When attempting to satisfy the many requirements for the creation of efficient transdermal delivery systems, polymer selection and design must be taken into account. The design of a polymer matrix poses the greatest challenge, which is then followed by optimisation of the drug-loaded matrix with regard to its cohesion-adhesion balance, physical and chemical properties, compatibility and stability with other system components as well as with skin. [4]

Main components in transdermal patch

- Enhancers of permeation from drugs
- Backing laminates
- release liners
- pressure-sensitive adhesive
- and other excipients such plasticizers and solvents

Components used in TDDS

Despite the fact that transdermal systems can be designed as any of the aforementioned many types of systems, the following fundamental ingredients are typically utilised in the formulations of practically all types of transdermal patches.

Drug: The drug for which the transdermal system is being developed should have specific physicochemical properties. Drugs should be water soluble (>100 mcg/ml), have a medium level of lipophilicity (log P 1-3.5), and have a reasonably low molecular weight (500 Dalton). Additionally, the medication needs to be a strong substance that works at low doses (20 mg).

Matrix : Drug is dissolved or disseminated in a polymer matrix when transdermal systems of the matrix type are being created. The polymer matrix in this matrix regulates the drug's release rate. Natural, manufactured, and semi-synthetic polymers, such as cellulose derivatives, pectin, sodium alginate, and chitosan, are all employed as polymers.

Reservoir: In this category of transdermal patches, a semi-permeable membrane is used to regulate the rate of medication delivery. In a reservoir, the medication is either liquid or solid.

Semipermeable (release) membrane: Used in multi-layer adhesive systems and reservoir-style transdermal systems. Membranes are made of cellulose nitrate, cellulose acetate, silicones, high-density polyethylene, polyester

elastomers, and ethylene-vinyl acetate copolymer. These membranes regulate how quickly medications are released.

Adhesive: The adhesive should make it simple for the transdermal system to stick to the skin and shouldn't irritate or cause skin allergies. Transdermal systems often use pressure-sensitive adhesives. The three groups of commonly used pressure-sensitive adhesives are acylates, polyisobutilene adhesives, and polysiloxan adhesives.

Backing layer: It guarantees the integrity of the system during storage and shields it from outside influences during administration. The backing layer is made of materials that are impervious to drug molecules for this purpose. The backing layer needs to be neutral and incompatible with the medication and other ingredients utilised in the formulation. Typically, backing layers consist of ethylene vinyl acetate, polyethylene, polypropylene, polyvinylidene chloride, and polyurethane.

Release liner: Removed prior to the system's adhesion to the skin, this component shields the formulation from the outside environment. You can use paper, aluminium foil, or ethylene vinyl acetate. In a perfect world, it would be simple to peel off the adhesive layer and wouldn't harm the adhesive layer's structure. Additionally, polymers made of silicone, fluorosilicone, and perfluorocarbon can be used.

Solvents , penetration enhancers : In order to dissolve or scatter the polymer, adhesive, or medication utilised in the preparation of the transdermal systems, a variety of solvents are used. Chloroform, methanol, acetone, isopropanol, and dichloromethane are among those that are widely utilised. Additionally, various penetration enhancers are added to the formulations to increase the drug's permeation through the skin. Terpenes, fatty acids, water, ethanol, glycols, surface-active compounds, azone, and dimethyl sulfoxide are frequently utilised in transdermal formulations as penetration enhancers.

Plasticizers : Plasticizers are utilised in transdermal systems to increase the polymer's brittleness and to offer flexibility.[5]

Evaluation of transdermal patches

Thickness uniformity : A Digimatic Micrometre (Mitutoyo, Japan) was used to measure the patch's thickness at various positions. Three samples from each formulation were randomly chosen, and the average of those three measurements was determined. From the mean value, the thickness standard deviations were calculated.

Weight variation: Three randomly chosen patches were separately weighed for the weight variation investigation. Each formulation should be subjected to such a determination. Each patch from each batch was weighed separately, and the average weight and standard deviation were computed.

Folding Stability : One patch was folded till it broke by folding it repeatedly in the same spot to test the folding endurance. The number of folds a patch may withstand at the same location before breaking indicates how durable folding is. All of the batches were subjected to this test.

Drug content uniformity : The patches were divided into pieces and put into a beaker with 100 millilitres of pH 7.4 phosphate buffered solution. Three patches from each batch were removed in order to examine the consistency of the medication in the patch. The medication was then extracted from each patch overnight by shaking it in a volumetric flask containing 100ml of phosphate buffered solution with a pH of 7.4. After an appropriate 10 ml dilution with phosphate buffered solution of pH 7.4, one millilitre of the resultant solution was removed and analysed UV-spectrophotometrically at 249 nm using phosphate buffered solution of pH 7.4. Three patches were chosen at random, and the drug content's mean and standard deviation were computed. For all of the batches, the same process was used, and drug content was recorded.

Tensile Power: The "Texture Analyzer" testing device was used to determine the Patch's tensile strength. There are two load cell grips in it. The upper one is adjustable, while the lower one is fixed. Between these cell grips, a test strip of a certain size was fastened before force was gradually applied until the patch broke. Directly from the dial reading, the Patch's tensile strength was calculated. By using the following equation, the tensile strength was determined. The standard deviation was estimated from mean data after three repetitions of the same method.

Tensile strength is calculated as Load at Failure / Area of Patch ×100.

Test for Percentage Moisture Loss: By storing the Films (2 x 2 cm2) in a desiccator containing anhydrous calcium chloride, the percentage of moisture loss was calculated.The Films were removed after 3 days, reweighed, and the % moisture loss was measured using the procedure below; Initial weight -Final weight / Initial weight× 100 equals the percentage of moisture loss.

% moisture absorption Test: The amount of moisture that was absorbed was calculated by storing the Films in a desiccator. To maintain 84% RH, a weighted film was removed from desiccators held at 40°C for 24 hours and subjected to a saturated potassium chloride solution. The films must be reweighed after 24 hours in order to calculate the percentage moisture uptake using the formula below.

Percentage of moisture uptake.=Final weight - Initial weight / Initial weight ×100[6]

Future of transdermal drug delivery system

Liposomes, niosomes, and micro emulsion are a few of the innovative formulation techniques and approaches of the future. The purpose of this method is to enhance the delivery of drugs with limited intrinsic solubility in the majority of excipients used in traditional formulations. Steroids, antifungal, antibacterial, interferon, methotrexate, and local anaesthetics are only a few examples of the many potential medications that could be delivered. Transdermal device sales are expected to grow in the future and have lately grown at a pace of 25% annually.Future technological advancements and an expanding list of transdermal drugs will result in an increase in this number. [7] As there are more advancements in design, transdermal distribution of analgesics is probably going to gain prominence. Research is being done to improve effectiveness and safety. To enable more precise medication distribution with an extended duration of action, as well as to improve practical aspects like the patch wearer's experience.[8] Improved transdermal technology that uses precise medication delivery and has a longer duration of action is another possible improvement. Improved transdermal technology, which either modifies the skin barrier or boosts the energy of the drug molecules, can increase drug flux across the skin by using mechanical energy. Following the development of iontophoresis-based patches, multiple 'active' transdermal technology modes are being researched for various medications.These include sonophoresis (which uses low-frequency ultrasonic energy to disrupt the stratum corneum), thermal energy (which uses heat to make the skin more permeable), and electroporation (which uses brief, high-voltage electrical pulses to temporarily create aqueous pores in the skin). The use of magnetic energy, or magnetophoresis, to boost medication flux over the skin has been studied. An underutilised method for managing both acute and chronic pain may be the transdermal patch. We anticipate that this method of drug delivery will become more widespread and applicable with enhanced delivery and a wider selection of analgesics. With about 40% of the drug delivery candidate products currently in clinical trials related to transdermal or dermal system, transdermal route of drug delivery system is currently the most successful innovative research area in new drug delivery system when compared to oral treatment. [9]

Conclusion

Since 1981, transdermal drug delivery systems have been utilised to give medications in a secure and efficient manner. Transdermal Patches have made significant advancements. Many researchers are interested in the Transdermal Drug Delivery System because of its significant benefits. Today, a lot of fresh research is being done to incorporate newer medications using this technique. Transdermal dose forms may give doctors the chance to give their patients more therapeutic options in order to improve their care. We now have a better knowledge of the nature of the stratum corneum barrier and how chemicals interact with and affect its structure thanks to the use of a number of biophysical approaches. Designing enhancers with the best characteristics and the least amount of toxicity will be made easier with a better understanding of how enhancers interact with the stratum corneum and the creation of structure-activity relationships for enhancers. In-depth information about transdermal drug delivery devices and its review procedure is provided in this article.

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