ISSN: 2230-7346

Saravanakumar K et al. / JGTPS / 6(1)-(2015) 2485 – 2490

(Review Article)

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

TRANSDERMAL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Transdermal drug delivery system is the system in which the delivery of the active ingredients of the drug occurs through the skin. Transdermal drug delivery can improve the therapeutic efficacy and safety of drugs because drug delivered through the skin at a predetermined and controlled rate. Skin is the important site of drug application for both local and systemic effect. The permeation of transdermal patches were crosses the skin through matrix and reservoir systems. Various techniques are available to prepare the transdermal patches such as solvent evaporation, solvent casting techniques. It provides more bioavailability when compared with the other route of administration respectively.

Keywords: Transdermal patch, Permeation Enhancer, Diffusion,Controlled Rate.

INTRODUCTION

Controlled medication release can be achieved by transdermal drug delivery systems (TDDS) which can deliver the drug via the skin portal to systemic circulation at a predetermined rate over a prolonged period of time[1-3]. For effective transdermal drug delivery system, the medication is effortlessly ready to penetrate the skin and effectively achieves the target site[4]. Transdermal drug delivery systems are gadgets containing medication of defined surface area that delivers a pre-determined amount of drug to the surface of intact skin at a predefined rate[5-6]. This system overcomes the disadvantages associated with oral products like first pass metabolism, diminished bioavailability, dosage dumping and dosing inflexibility[7-8]. The system is for the most part non-obtrusive so it is all around acknowledged by patients and can be utilized to give neighborhood and additionally systemic conveyance more than a few days [9-10].

Plasticizers are added to polymeric framework to alter their physical properties and to enhance their film shaping glycol subordinates attributes. Plasticizers can change the visco-elastic conduct of polymers together[11-12]. Plasticizers can transform a hard delicate polymer into a milder, more malleable material and potentially make it more impervious to mechanical stress. The plasticizer will mediate itself between the polymer chains and communicate with the strengths held together by enlarging and softening the polymer framework[13].

Most of the transdermal candidates have low permeability. The drugs administered across the skin should have the three constraining characteristics: appropriate partition coefficient, low molecular mass (<500Da) and small required dose (up to milligrams). The limitations of transdermal drug delivery are caused by skin which protects against and is impermeable to foreign molecules[14-15]. The human skin is consisted of two main layers like the layer of epidermis and the layer of dermis. Stratum conium is the epidermis's outermost layer that composed of stratified keratinocytes, multiple lipid bilayers of ceramidas, fatty acids, cholesterol and cholesterol esters. Stratum cornium provides an extremely effective physical barrier for the control of drug penetration in to the skin[16].

Structure of Skin

The human skin is a muti layered organ composed of many histological layers. Skin is most accessible organ in body. Its major functions are; protection of major or vital internal organs from the external influences, temperature regulations, control of water output and sensation. The skin of an average adult body covers approximately surface area of two square meters and receives about one-third of the blood circulating through the body. Skin serves as the point of administration for systemically active drugs, the drug applied topically will be absorbed, first into the systemic circulation and then transported to target tissues[17].

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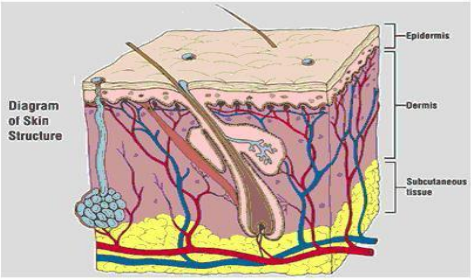

Figure No.1. Diagram of Skin Structure

Epidermis

The epidermis is a stratified, squamous keratinizing epithelium. The keratinocytes involve the major cell segment (>90%) and the responsible for the evolution of barrier function. Keratinocytes change their shape, size and physical properties when moving to the skin surface. Different cells present which are show in this layer incorporate melanocytes, langerhans cells and markel cells, none of which seems to add to the physical parts of the barrier. Minutely, the epidermis further partitioned into five anatomical layers with stratum corneum shaping the external most layer of the epidermis, presenting to the outside environment. Stratum cornium is the peripheral layer of epidermis pretty nearly 100-150 micrometers thick, has no blood stream. This is the layer most critical to transdermal conveyance as its structure permits it to keep water inside the body and remote substances out[18].

Dermis

The dermis is the internal and bigger (90%) skin layer, involves principally of connective tissue and gives backings to the epidermis layer of the skin. The limit in the middle of dermis and epidermis layer is called dermal- epidermal intersection which gives a physical obstruction to the vast particles of medication and cells. The dermis joins blood and lymphatic vesicles and nerve endings. The far reaching microvasculature system which is found in the dermis speaks to the site of resorption for medications consumed over the epidermis. The dermis can be partitioned into two anatomical district, papillary dermis and reticular dermis. intersection. As skin is main consideration for the determination of different medication conveyance perspectives like saturation and retention of medication over the dermis[19].

Hypodermis

The hypodermis is the fat tissue layer which is found in the middle of dermis and aponeurosis and fasciae of the muscles. The subcutaneous fat tissue is fundamentally and practically is all around coordinated with the dermis through the nerve and vascular systems. The hypodermis layer is made out of free connective tissues and its thickness differs as per the surface of body [20].

Advantages[21-22]

- Improved bioavailability.
- More uniform plasma levels and keep up plasma amassing of intense Medication.
- Reduced reactions and enhanced treatment because of support of plasma levels up to the end of the dosing interim.
- Flexibility of ending the medication organization by just expelling patch from the skin. Improved patient consistence and solace by means of non-obtrusive, easy and basic application.
- Avoid bury and intra understanding variety and upgrade remedial viability.

Disadvantages[23-24]

- Many sedates particularly tranquilizes with hydrophilic structures saturate the skin too gradually to be of helpful advantage.
- The obstruction capacity of the skin changes starting with one site then onto the next on the same individual, from individual to individual furthermore with age. Only little, lipophilic medications can be conveyed at present through the skin.
- Drug particle must be strong in light of the fact that fix size breaking points sum that can be conveyed.
- Not suitable for high medication dosages.
- Adhesion may shift with patch sort and natural conditions.
- Skin disturbance and excessive touchiness responses may happen.
- Drugs that oblige high blood levels can't be managed. Along with these impediments the high cost of the item is likewise a significant down side.

ENHANCERS OF TDDS

Enhancers build the infiltration of permeation by disturbing the structure of skin's external layer i.e stratum cornium and expanding penetrant dissolvability. Disturbance either by the method for compound which may influence both the intracellular and extracellular structure. Interruption may be because of protein denaturation, fluidization and randomization of intercellular lipids or intercellular delamination and extension. Enhancers[25] of transdermal medication conveyance framework are physical enhancers, particulate frameworks, and chemical enhancers.

Particulate framework

The enhancers of transdermal medication conveyance sytem are liposomes, microemulsion, transfersome, noisomes and nanoparticles are the cases of particulate method for upgrade.

Physical enhancers

The enhancers of transdermal medication conveyance framework are the iontophoresis, electroporation, magnetophoresis, microneedle and ultra sound (otherwise called phonophoresis or sonophoresis) methods are illustrations of physical method for improvement that have been utilized for upgrading percutaneous entrance (and retention) of different sorts of remedial specialists.

Chemical enhancers

The enhancers of transdermal medication conveyance framework by method for chemicals are sulphoxides, glycols, alkanols, terpenes, and so forth. Chemicals that advance the infiltration of topically connected medications are generally alluded to as accelerants, retention promoters, or entrance enhancers.

IDEAL PROPERTIES[26-28] OF TDDS

The perfect properties of transdermal medication conveyance framework are;

Optimum part coefficient needed for the helpful activity of medication.

Shelf life up to 2 years.

Low dissolving purpose of the medication is sought which is under 200^{o}C.

Patch size ought to be <40cm^{2}.

The pH of the soaked arrangement is to be between 5-9.

PARTS[29]OF TDDS

Drug- Drug arrangement has a direct contact with the discharge liner.

Permeation enhancers-increase the infiltration of the medication.

Polymer network/drug supply.

Pressure touchy cement adhesive like Acrylic, Polyisobutylene, silicon serves to follow the segments of the patch together alongside following the patch of the skin.

Backing overlays the film shields the patch from the outside environment.

Release internal and different excipients like plasticizers and different solvents. Liner secures the patch amid capacity.

Membrane- Membrane controls the arrival of medication from the store.

TYPES[30] OF TRANSDERMAL PATCHES

Single layer medication in adhesive

In this kind of the cement layer contains the medication. The glue layer not just serves as to follow the different layers together furthermore in charge of discharging the medication to the skin. The glue layer is encompassed by a provisional liner and a support.

Multi-layer medication in adhesive

This sort is additionally like the single layer yet it contains a quick medication discharge layer and other layer will be a controlled discharge alongside the cement layer. The cement layer is in charge of discharging of the medication. This patch additionally has an interim liner-layer and a perpetual support.

Vapor patch

In this kind of patch the part of cement layer not just serves to follow the different layers together additionally serves as discharge vapor. The vapor patches are new to the business sector, usually utilized. Different sorts of vapor patches are likewise accessible in the business sector which are utilized to enhance the nature of slumber and lessens the cigarette smoking conditions.

Reservoir system

In this framework the medication repository is inserted between an impenetrable sponsorship layer and a rate controlling film. The medication discharges just through the rate controlling film, which can be permeable or nonporous. In these medication store compartment, the medication can be as an answer, suspension, gel or scattered in a strong polymer grid. Hypoallergenic glue polymer can be connected as external surface polymeric layer which is perfect with the medication.

Drug in adhesive system

In this sort of the medication store is framed by scattering the medication in a glue polymer and afterward spreading the sedated glue polymer by dissolvable throwing or liquefying an impenetrable support layer. On top of the repository, unmediated glue polymer cement polymer layers are petitioned security reason.

Matrix-dispersion system

In this kind of the medication is scattered homogenously in a hydrophilic or lipophillic polymer grid. This medication containing polymer plate is altered on to an occlusive base plate in a compartment manufactured from a medication impermeable sponsorship layer. As opposed to applying of glue on the substance of the medication. It is spread alongside the circuit to frame a piece of cement edge.

Micro reservoir system

In this kind of the medication conveyance framework is a mix of repository and grid scattering framework. The medication store is framed first by suspending the medication in a watery arrangement of water dissolvable polymer and after that scattering the arrangement homogeneously in a lipophilic polymer to shape a large number of inaccessible, infinitesimal circles of medication stores. At that point thermodynamically unsteady scattering is settled rapidly by instantly cross-connecting the polymer in situ by utilizing cross connecting operators[31-32].

APPLICATIONS OF TRANSDERMAL PATCHES

Transdermal patch of the nicotine, which discharges nicotine in controlled measurements to help with suspension of tobacco smoking.

Nitroglycerine patches are likewise some of the time recommended for the treatment of the Angina pectoris.

Clonidine, the antihypertensive medication and ketoprofen, the non-steroidal anti-inflamatory medication are likewise accessible as transdermal patches.

Transdermal manifestation of the MAOI selegiline, turned into the first transdermal conveyance operaters for a stimulant.

Transdermal medication conveyance operators for the attention deficit hyper disorder.

EVALUATION TESTS

Drug content determination

An accurately weighed portion of film is dissolved in 100 ml of solvent in which the drug is soluble and then the solution is shaken continuously for 24 hr in shaker incubator. Then the whole solution is sonicated. After incubation and subsequent filtration, drug in solution is estimated by spectrophotometrically at appropriate dilution.

Percentage Moisture content

The prepared films are weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 hr. The films are weighed again after specific intervals until they show a constant weight. The percent moisture content is calculated by using the formula.

Percentage moisture content =

Initial weight –Final weight /final weight ×100

Percentage moisture uptake

Weighed movies are to be taken in a dessicator at room temperature for 24 hr. These are then taken out and presented to 84% relative moistness utilizing soaked arrangement of potassium chloride in a desicator until a consistent weight is attained to. Rate dampness uptake is ascertained by utilizing the equation.

Percentage moisture uptake= Final weight- Initial weight/ Initial weight X 100

Water vapor penetrability assessment (WVP)

Water vapour porousness can be resolved with froth dressing system the air constrained broiler is supplanted by a characteristic air dissemination stove. The WVP can be controlled by the accompanying equation**.**

$$WVP = W/A$$

Where, WVP is communicated in gm^2 every 24 hr,

W is the measure of vapor penetrated through the patch.

Folding Endurance

A piece of particular region is to be cut uniformly, over and over collapsed at the same spot till it broke. The quantity of times the film could be collapsed at the same spot without breaking gave the estimation of the folding endurance.

Thickness of the patch

The thickness of the patch which is drug loaded is measured at different points by using a screw gauge and determines the average thickness and standard deviation of the prepared patch.

Flatness

A transdermal patch should have a smooth surface and should not constrict with time. This can be demonstrated by flatness study. For flatness study, one strip is cut from the centre and two from each side of patches. The length of the each strip is measured and variation in length is calculated by determining percent constriction. 0% constriction is equivalent to 100 % flatness.

Weight variation

The arranged patches are dried at 600ºc for 4hr preceding testing. A predefined territory of patch is to be cut in diverse parts of the patch and say something computerized equalization. The normal weight and standard deviation qualities are to be calculated from the individual weights.

***In-vitro* permeation**

The *in-vitro* permeation investigation of created transdermal patches was done by utilizing a rodent stomach skin and franz diffusion cell. The skin was sandwiched in the middle of contributor and receptor compartments of the franz diffusion cell. A 2.2 cm measurement of the patch was set in close contact with the stratum cornium side of the skin, the top side was used as a support film spread with aluminum.Teflon dot was set in the receptor compartment loaded with 12 ml of ordinary saline. The cell substances were blended in an attractive stirrer at a temperature of 37 ± 5°C was kept up all through the test. 1ml of test sample was withdrawn through the testing port at distinctive time intervals for a time of 24 h, all the equivalent volume of phosphate buffer pH 7.4 after every withdrawal. At that point the samples were investigated by using spectrophotometrically[33-34].

Stability studies

The steadiness studies are behavior to explore the impact of temperature and relative dampness on the medication content in diverse definitions. The transdermal plans are subjected to solidness contemplates according to ICH rules[35-36].

CONCLUSION

Tansdermal medication conveyance framework is helpful for topical and neighborhood activity of the medication. Because of extensive points of interest of the Transdermal Drug Delivery System and different saturation enhancers which would fundamentally expand the quantity of medications suitable for Transdermal medication conveyance framework; this framework intrigues a ton of scientists. Transdermal Drug Delivery System a sensible functional application as the up and coming era of medication conveyance framework.

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How to cite this article:

Saravanakumar K, Swapna P, Vani.P, Pujitha K, Transdermal drug delivery system: a review, 6(1): 2485 - 2490. (2015)