International Journal of

Innovative Drug Discovery

e ISSN 2249 - 7609
Print ISSN 2249 - 7617

www.ijidd.com

TRANSDERMAL DRUG DELEVERY SYSTEM-A REVIEW

Ankith Kumar Reddy B*, Subhashis Debnath, M. Niranjan Babu

Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh- 517 561, India.

ABSTRACT

Transdermal drug delivery has achieved a great importance in the formulation of drug delivery systems which are highly lipophilic in nature as the skin can allow the lipophilic drugs even though having a dead tissue called stratum corneum which is rate limiting step in the drug release but it can be overcome by the usage of penetration enhancers in the formulation. Drugs having short half-life are best suited for transdermal drug delivery system. In this review it has clearly mentioned about the different methods by which TDDS can be formulated.

KEY WORDS: stratum corneum, skin, permeation.

INTRODUCTION

Human skin has a multifunctional role, primary among which is its role as a barrier against both the egress of endogenous substances such as water and the ingress of xenobiotic material (chemicals and drugs). This barrier function of the skin is reflected by its multilayered structure. The top or uppermost layer of the skin known as the stratum corneum (SC) represents the end product of the differentiation process initially started in the basal layer of the epidermis with the formation of keratinocytes by mitotic division. The SC, therefore, is composed of dead cells (corneocytes) interdispersed within a lipid rich matrix. It is the "brick and mortar" architecture and lipophilic nature of the SC, which primarily accounts for the barrier properties of the skin. The SC is also known to exhibit selective permeability and allows only relatively lipophilic compounds to diffuse into the lower layers. As a result of the dead nature of the SC, solute transport across this layer is primarily by passive diffusion in accordance with Fick's Law and no active transport processes have been identified.

Typical delivery systems can be utilised to achieve transdermal drug delivery or dermal drug delivery. Barrier in order that they exert a systemic effect whereas the latter refers to delivery of drugs to particular locations within the skin so that they exert a local effect. This sort of dermal drug delivery approach is commonly used in the treatment of dermatological conditions such as skin cancer, psoriasis, eczema and microbial infections, where the disease is located in the skin. Like many alternative routes of delivery, the skin has both benefits and limitations when compared with more conventional methods such as oral drug delivery. In the last 25 years numerous methods of overcoming the skin barrier have been described, but they can broadly be divided into two main categories defined as either passive or active methods [1].

TYPES OF TRANSDERMAL PATCHES

a) Single layer drug in adhesive

In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and also responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

b) Multi -layer drug in adhesive

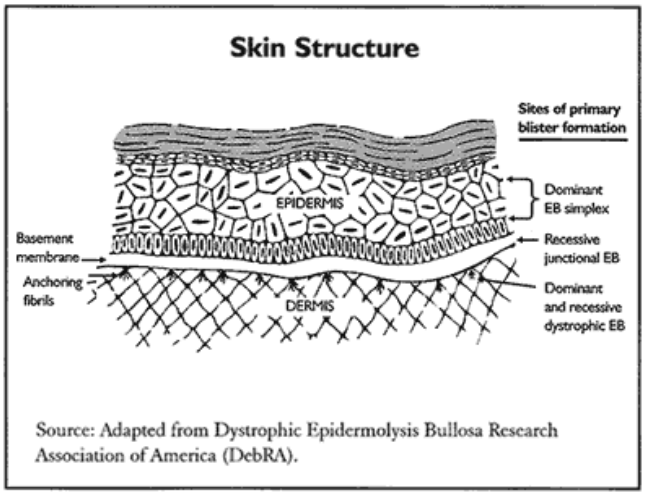
This type is also similar to the single layer but it contains aim mediate drug release layer and other layer will be a controlled release along with the adhesive layer. The adhesive layer is responsible for the releasing of the drug. This patch also has a temporary liner-layer and a permanent backing.

c) Vapour patch

In this type of patch the role of adhesive layer not only serves to adhere the various layers together but also

Corresponding Author:- **Ankith Kumar Reddy.B** Email:-: ankithpharmaline0002@gmail.com

serves as release vapour. The vapour patches are new to the market, commonly used for releasing of essential oils in decongestion. Various other types of vapor patches are also available in the market which are used to improve the quality of sleep and reduces the cigarette smoking conditions.



d) Reservoir system

In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or nonporous. In the drug reservoir compartment, the drug can be the form of a solution, suspension, gel or dispersed in a solid polymer matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymeric membrane which is compatible with drug

e) Matrix system

Drug-in-adhesive system

In this type the drug reservoir is formed by dispersing the drug in an adhesive polymer and then spreading the medicated adhesive polymer by solvent casting or melting(in the case of hot-melt adhesives) on an impervious backing layer. On top of the reservoir, unmediated adhesive polymer layers are applied for protection purpose.

Matrix-dispersion system

In this type the drug is dispersed homogenously in a hydrophilic or lipophilic polymer matrix. This drug containing polymer disk is fixed on to an occlusive baseplate in a compartment fabricated from a drug impermeable backing layer. Instead of applying the adhesive on the face of the drug reservoir, it is spread along with the circumference to form a strip of adhesive

f) Micro reservoir system

In this type the drug delivery system is a combination of reservoir and matrix-dispersion system. The drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unreachable, microscopic spheres of drug reservoirs. This thermodynamically unstable dispersion is stabilized quickly by immediately cross-linking the polymer in situ by using cross linking agents [2-4].

Micro needles

Microfabricated micro needles are devices which are hybrids of the hypodermic needle and transdermal patch through the use of microscopic needles that can deliver the drug effectively (like a hypodermic needle). Their small size offers the potential advantages of delivering large molecules across the *stratum corneum* without extreme pain to the patients. The first micro needles systems consisted of a drug reservoir and a plurality of projections (micro needles) extending from the reservoir, which penetrate the stratum corneum and epidermis to deliver the drug. The micro needle concept employs an array of micron-scale needles that can deliver drug into the epidermis and dermis, which ultimately leads to uptake by the capillaries for systemic delivery but not so far that micro needles hit the nerves. This is the reason for the device being less painful to patients. The most common material used for micro fabrication of needles is silicon. These micro needles have extremely sharp tips(radius of curvature, <1μm) that facilitate easy piercing of the skin. Individual silicon needles measuring approximately 150 μm in length and with 80 μm base diameter are fabricated onto arrays of approximately 400 microneedles (approx. 3 X 3 mm). Needles with hollow centers have also been produced, each containing a bore of 5-70 μm (depending on the required design) through which drug can be administered. A broad range of compounds such as calcein (623 Da), insulin (6000Da), BSA (66000Da) and polymeric nanoparticles are delivered at significant rates through skin permeabilized by micro fabricated micro needles.

Iontophoresis: Iontophoresis may be defined as the facilitation of ionizable drug permeation across the skin by an applied electrical potential, the driving force of which may be simply visualized as electrostatic repulsion. A typical iontophoresis device consists of a battery, microprocessor controller, drug reservoir and electrodes. The technique involves the application of a small electric current (usually 0.5 mA/cm2) to a drug reservoir on the skin, with the similarly charged electrodes (on the surface of the skin) placed together in the drug reservoir producing are pulsion effect that effectively drives the solute molecules away from the electrode and into the skin. There are three explanations of how iontophoresis increases transdermal drug delivery. The first, proposes that the drugs are forced across the skin by simple electronic repulsion of similar

charges. Anionic drugs can cross the skin by using a negatively charged electrode. Similarly cationic drugs enter the skin more successfully when a positively charged electrode is used. The second, explanation suggests that the electric current enhances permeation by inhibiting the skin's ability to perform its protective barrier function. The third, states that iontophoresis causes water, a very effective penetration enhancer, to enter the stratum corneum by electro-osmosis. Dissolved drugs can be carried across the skin along with the penetrating water during iontophoresis. At physiological pH, human skin has slight negative charge; therefore, certain cationic drugs can more easily cross the skin during iontophoresis due to reduced resistance. Several studies have addressed the application of iontophoresis to the delivery of low molecular weight solutes (< 500 Da). For delivery of macromolecules, proteins and peptides such as calcitonin, corticotrophin-releasing hormone, δ-sleep-inducing peptide, dextrin sulphate, inulin, insulin, gonadotropin releasing hormone, growth hormone releasing factor, neutral thyrotrophin releasing hormone, parathyroid hormone and vasopressin iontophoresis may also be utilized. To date, clinical studies have been limited to smaller molecules such as lidocaine, ketorolac dexamethasone, etofenamate, naproxen, vincristine, cortisone and fentanyl [5].

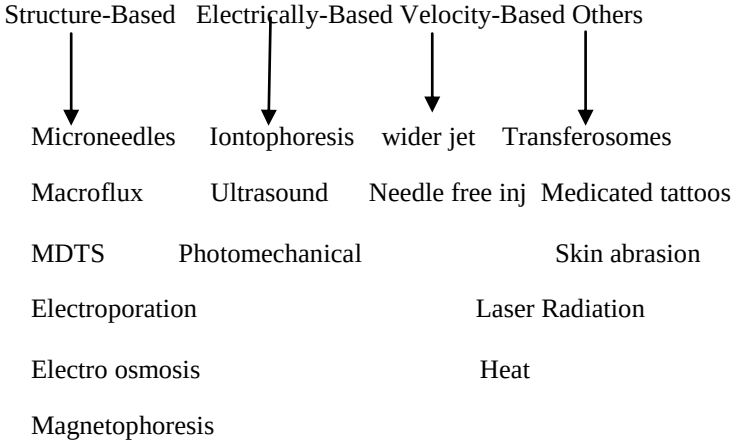
Electroporation

This method involves the application of high voltage pulses to the skin, which has been suggested to induce formation of transient pores. High voltages in the form of direct current [DC(100 volts)] caused by electrical pulses with short treatment durations (milliseconds) are most frequently employed. Other parameters that affect delivery include pulse properties such as wave form, rate and number. The mechanism of penetration is the formation of transient pores due to electric pulses that subsequently allow the passage of macromolecules from the outside of the cell to the intracellular space via a combination of possible processes such as diffusion and local electrophoresis. The electrical resistance of the skin is reported to drop as much as three orders of magnitude within microseconds of administration of an electric pulse. The technology has been successfully used to enhance the skin permeability of molecules with differing lipophilicity and size (i.e., small molecules, proteins, peptides and oligonucleotides)including biopharmaceuticals with molecular weights greater than 7Kda.Increase in transdermal penetration of up to 104fold have been reported *in vitro* for various sizes of molecules such as metoprolol, lidocaine, tetracaine, vitamin C, timolol and fentanyl dyes, including calcein and methylene blue, and macromolecules up to 40 KDa including cyclosporine A, heparin, luteinising hormone releasing hormone, insulin, oligonucleotides and dextrans (MW 4.4 – 39 KDa)

Ultrasound

Ultrasound (sonophoresis, phonophoresis and ultraphonophoresis) is a technique for increasing the skin permeation of drugs using ultrasound (20 KHZ to 16 MHZ) as a physical force. It is a combination of ultrasound therapy with topical drug therapy to achieve therapeutic drug concentrations at selected sites in the skin. In this technique, the drug is mixed with a coupling agent usually a gel but sometimes a cream or ointment is used which transfers ultrasonic energy from the device to the skin through this coupling agent. Application of low – frequency ultrasound (20 -100 KHZ) enhances skin permeability more effectively than high – frequency ultrasound (1 -16 MHZ). The mechanism of transdermal skin permeation involves disruption of the stratum corneum lipids, thus allowing the drug to pass through the skin. A corresponding reduction in skin resistance was observed due to cavitation, micro streaming and heat generation. Reverse ultrasound technology may also be used for the extraction of interstitial fluid samples for analysis [6].

Fig 1. Recent techniques based on active transport for enhancing TDDS. RECENTT TECHNIQUES OF ENHANCING TDDS



REFERENCES

1. Langer R. Transdermal drug delivery: past progress, Current status, and future prospects. *Advanced Drug Delivery Reviews,* 56, 2004, 557-58.
2. Prausnitz MR, Mitragotri S, Langer R. Current status and future potential of transdermal drug delivery. *Nature Reviews,* 3, 2004, 115-24.
3. Jain N, Talegonkar S, Jain NK. New ways to enter the blood stream: Emerging strategies in transdermal drug delivery. *The Pharma Review,* 2004, 41-59.
4. Barry B. Transdermal drug delivery. In: Aulton EM. Pharmaceutics, The science of dosage forms design, 2nd ed, Churchill Livingstone, Newyork, Harcourt publishers, 2002, 499-33.
5. Ansel HC, Loyd AV, Popovich NG. Pharmaceutical dosage system, 7th ed, Lippincott Williams and Willkins publication.
6. Chien YW. Transdermal drug delivery and delivery system. Marcel Dekker, Inc. New York, 50, 1992, 301-381.