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Transdermal Drug Delivery System: A Review

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ABSTRACT

Although transdermal drug administration has made a significant contribution to medical practise, it has yet to realise its full potential as an alternative to oral drug delivery and hypodermic injections. The patch can essentially provide a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive, which is an advantage of transdermal drug delivery over other types of delivery systems such as oral, topical, intravenous, intramuscular, and so on. The clinical usage of first-generation transdermal delivery systems for the delivery of tiny, lipophilic, low-dose medicines has increased steadily. Chemical enhancers, non-cavitational ultrasound, and iontophoresis have all been used in second-generation delivery methods.

KEYWORDS: *Study of Transdermal Drug Delivery System, Approches of Transdermal Patches, Recent Advances in Transdermal Patches*

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INTRODUCTION

TRANSDERMAL DRUG DELIVERY SYSTEM:

Transdermal delivery systems (TDS) or transdermal therapeutic systems are topical formulations comprising medicines with systemic effect (TTS). The distribution of a medicine through 'intact' skin so that it reaches the systemic circulation in sufficient quantity to be useful following administration of a therapeutic dose is known as transdermal delivery. Transdermal systems are appropriate for disorders that need to be treated on a long-term basis. As a result, anti-diabetic medicines used for both therapeutic and preventive purposes have been investigated transdermally.

Advantages:

A. Prevents gastrointestinal medication absorption problems caused by gut pH, enzymatic activity, and drug interactions with food, drink, and other orally administered drugs.

B. Can be used to replace oral pharmaceutical delivery when the route is not suitable, such as in the case of vomiting or diarrhoea.

C. To prevent the first-pass effect, such as with Transdermal Nitroglycerin. When taken orally, it is rapidly metabolised by the liner.

D. Noninvasive, as opposed to parenteral therapy, which is inconvenient.

E. They provided longer therapy with a single application, resulting in better compliance than alternative dosage forms that required more frequent dose administration, such as transdermal clonidine 7 day.

F. The activity of medications with a short half-life is prolonged by the presence of a drug reservoir in the therapeutic delivery system and its controlled release. g) Drug therapy may be necessary.

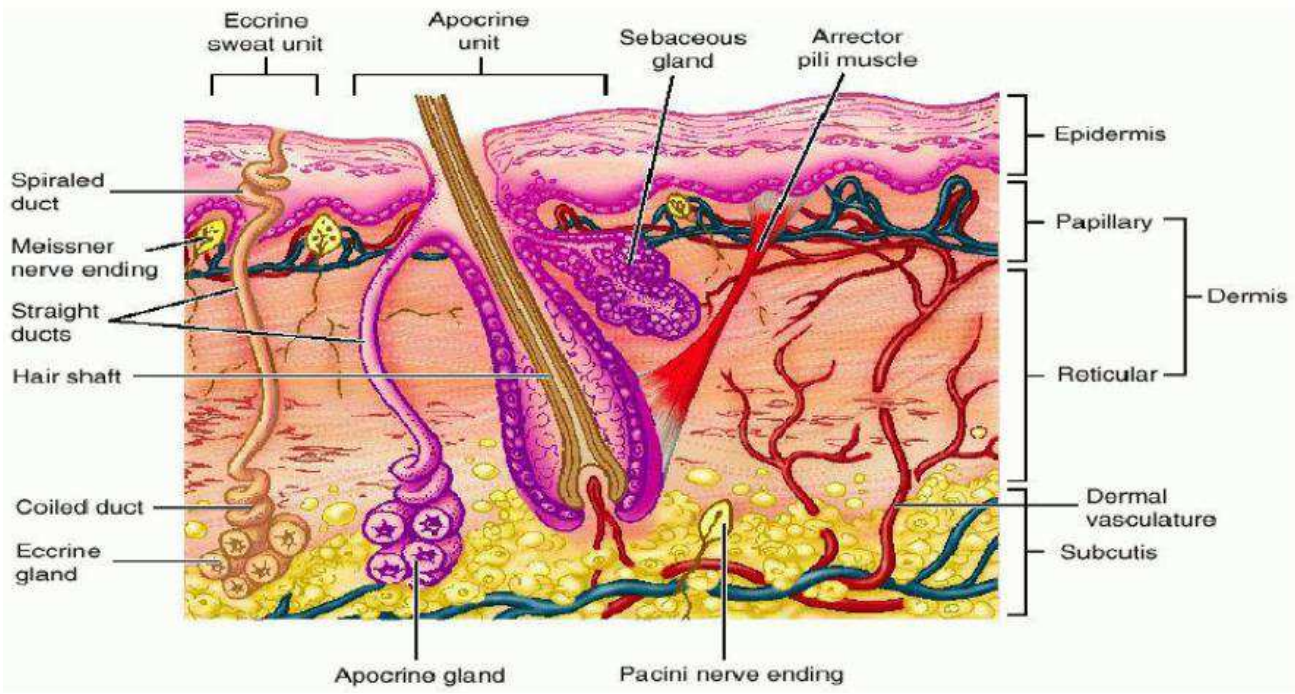

Figure 1: Anatomy of Skin

Disadvantages:

A. Contact dermatitis from one or more of the system components causes contact dermatitis at the application site, prompting termination 1.
B. Because of the natural limits of drug entrance imposed by the skin's impermeability, only powerful medicines are suitable candidates for transdermal patch.
C. Some medications, such as the scopolamine transdermal patch worn behind the ear, are unpleasant.
D. It's difficult to stick to a long period of time.

ANATOMY AND PHYSIOLOGY OF SKIN:

The skin has evolved into a highly effective barrier that inhibits both excessive water loss and xenobiotic invasion. It gives us the ability to tolerate a wide range of environmental difficulties. The reasons behind this are numerous, but for the sake of this chapter, they can be stated briefly. Almost all substances have a rate-controlling barrier in the stratum corneum, which is the outer layer of the skin. Corneocytes, which are dead, flattened, keratin-rich cells, make up this structure.

These packed cells are surrounded by a complicated intercellular lipid combination. Ceramides, free fatty acids, cholesterol, and cholesterol sulphate are among them. The fact that they are organised into categories is the most crucial characteristic.

(1.4 g/cm2 in dry state) and low moisture of 15 to 20 percent, the skin, particularly the stratum corneum, acts as a barrier to medication penetration. The barrier function is aided further by the replacement of the stratum corneum on a regular basis, lowering topical and transdermal absorption. As a result, various studies in the domain of penetration enhancement have been done in recent years3. Slow penetration rates, a lack of dosage flexibility, and a restriction to relatively low dosage medicines are all drawbacks. 4. Human skin is made up of three separate but interdependent tissues.

PRINCIPLES OF TRANSDERMAL PERMEATION:

Previously, skin was thought to be an impenetrable protective barrier, but subsequent research has demonstrated the value of skin as a route for systemic administration. Because only a fraction of a millimetre of tissue separates the surface of the skin from the underlying capillary network, it is the most intensive and easily accessible organ in the body. The following are the numerous processes involved in drug transport from the patch to the systemic circulation: 5: 1. Drug diffusion from the drug reservoir to the rate-regulating membrane. 2. Drug diffusion from the rate-limiting membrane to the stratum corneum. 3. Sorption through the stratum corneum and penetration through the epidermis that is still alive. 4. Drug uptake by the dermal papillary layer's capillary network. 5. Impact on the organ of interest

KINETICS OF TRANSDERMAL PERMEATION:

The ability to understand skin penetration dynamics is critical for the creation of successful transdermal medicinal devices. The steps involved in transdermal penetration of a medication are as follows:

1. Sorption through the stratum corneum 2. Drug penetration through the epidermis. 3. Drug uptake in the dermal papillary layer via the capillary network.

Only if the medicine has specific physiochemical qualities will it be able to permeate the body. The rate of permeation across the skin is calculated as follows: dQ/dt = Ps (Cd– Cr), where Cd and Cr are the concentrations of the skin penetrant in the donor compartment, i.e. the stratum corneum surface, and the receptor compartment, i.e. the body, respectively. Ps is the skin tissue's total permeability coefficient to the penetrant. The permeability coefficient is calculated using the

For a skin penetrant, the coefficient Ps can be assumed constant. It is obvious from the preceding equation that a constant rate of drug permeation can be achieved only when Cd >> Cr, that is, when the drug concentration at the stratum corneum's surface Cd is continuously and significantly more than the drug concentration in the body Cr. dQ /dt= Ps Cd becomes the equation. If the magnitude of Cd is generally constant over the period of skin permeation, the rate of skin permeation is constant. The drug should be released from the device at a rate Rr, which is either constant or greater than the rate of skin uptake Ra, i.e. Rr >> Ra, to keep Cd constant. Since Rr > Ra, the drug concentration on the skin is higher.

BIOPHARMACEUTICA L PARAMETERS IN TRANSDERMAL PATCH 7 DRUG SELECTION:

The dose should be kept modest, around 20mg per day. The half-life should be shorter than 10 hours. The molecular weight of the compound should be 400. The partition coefficient should be between 1.0 and 4 Log P (octanolwater). The permeability coefficient of the skin should be 0.5 X 103cm/h. The drug should not irritate or sensitise the skin in any way. Bioavailability in the mouth should be low. The therapeutic index should be as low as possible.

APPROACHES USED IN DEVELOPMENT OF TRANSDERMAL PATCH5:

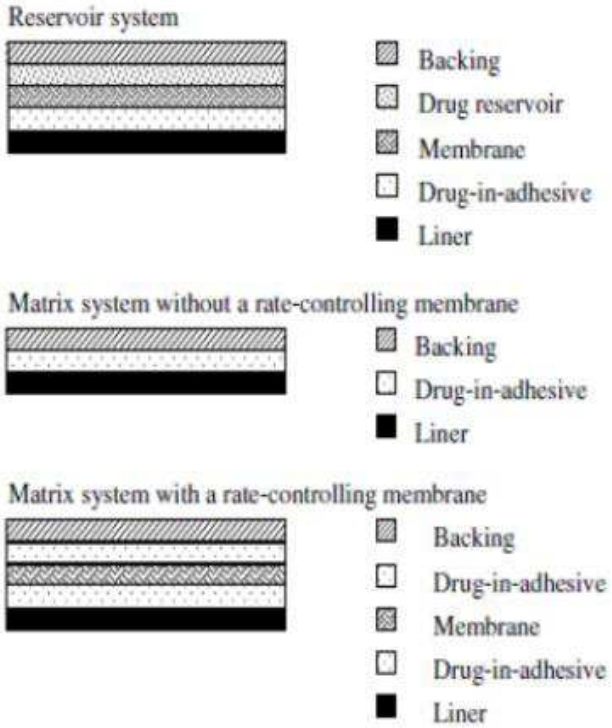

Figure 2 Types of TDDS

A. Membrane moderated systems:

In this, the drug reservoir is totally encapsulated in a shallow compartment molded from a drug impermeable metallic plastic laminate and a rate controlling polymeric membrane. In the drug reservoir compartment, the drug solids are either dispersed in a solid polymer matrix or suspended in an unleachable, viscous liquid medium e.g. silicon fluid. The rate controlling membrane can be micro

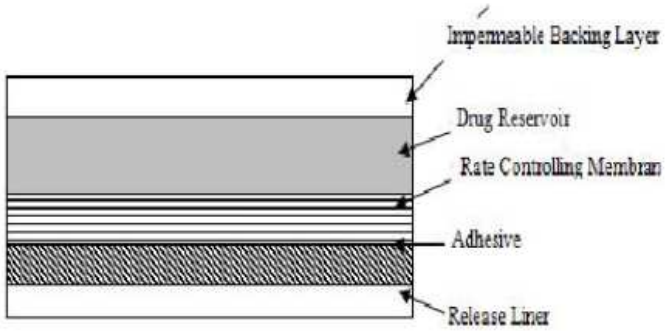

Figure 3 Representation of Membrane moderated systems

A skin layer of medication, suitable hypo allergic sticky polymer, or a porous or nonporous polymeric membrane e.g. ethylene vinyl acetate copolymer on the external surface of the polymeric membrane may be applied to produce an intimate contact of TDDS with the skin surface. TransdermNitro is a once-daily system; TransdermScop is a three-day medicine system; Catapres TTS is a weekly treatment system.

B. Adhesive diffusion controlled system:

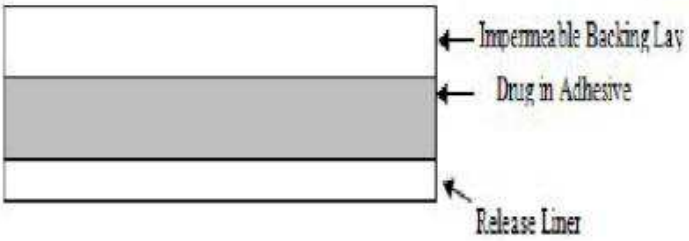

Figure 4 Representation of adhesive diffusion controlled system

It's the most basic version of membrane-moderated drug delivery devices. The drug reservoir is created in this technique by dispersing the drug directly in an adhesive polymer and then solvent casting the medicated adhesive onto a flat sheet of drug impermeable metallic plastic backing to generate a thin drug reservoir layer. Layers of nonmedicated rate regulating sticky polymer of consistent thickness are put on top of the reservoir layer. Single-layer or multi-layer drug-in-adhesive patches are available. The multi layer system differs from the single layer method in that it includes an additional layer of drug-in-adhesive, normally separated by a membrane. Due of the convenience of remembering once weekly, pharmacological characteristics in adhesive patches may account for increased patient compliance.

C. Matrix dispersion:

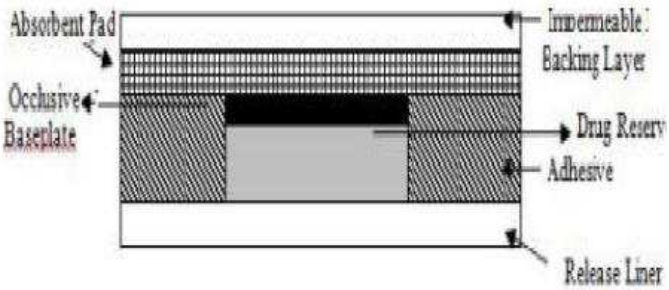

Figure 5 Representation of matrix dispersion

The drug reservoir is created by dispersing the drug particles uniformly in a hydrophilic or lipophilic polymer matrix, and then moulding the medicated polymer into a disc with a predetermined area and thickness. The adhesive polymer is dispersed along the circumference of the disc to produce a stripe of adhesive rim around it, and it is attached onto an occlusive base plate on the disc's surface.

The absence of dosage dumping, direct exposure of polymeric matrix to the skin, and lack of adhesive interference are all advantages of matrix patches.

D. Microreservoir system

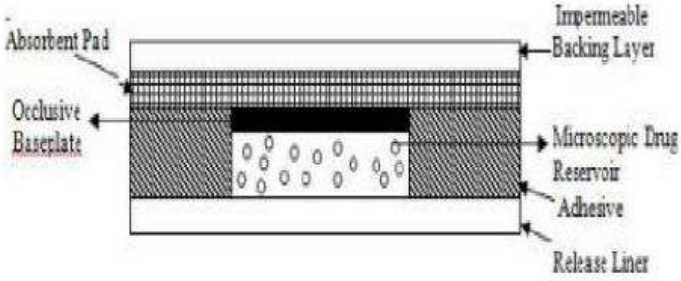

Figure 6 Representation of microreservoir system

These are classified as a mix of reservoir and matrix dispersion. The drug reservoir is created by suspending the drug particles in an aqueous solution of a water soluble polymer and then homogeneously dispersing the drug suspension in a lipophilic polymer using high shear mechanical force to form unleachable microscopic spheres of drug reservoir. This dispersion is quickly stabilised by cross linking the polymer chains, resulting in a medicated disc with a consistent surface area and thickness. System that is marketed: Nitrodisc®

ADVANCES IN THE FIELD OF TRANSDERMAL PATCHES RECENTLY:

There have been several research projects in this sector, and just a few are now underway.

The following are some of the most recent studies in the realm of transdermal patches:

- Protein delivery via patch technology:

Large amounts of medication can be delivered through the skin. The skin's living tissues, diffusing across a strong concentration gradient8.

- Pain-free diabetic monitoring using transdermal patches:

The initial prototype patch is around 1cm in diameter and is constructed of polymers and thin metallic sheets. The 55 sampling array, as well as their metallic connectors, can be seen clearly. When the skin's seal is broken, the interstitial fluid and the biomolecules it contains become visible on the skin's surface. A high-temperature heat pulse can be applied locally, breaching the stratum corneum, using microheating devices embedded into the structural layer of the patch nearest to the skin surface. The skin surface is exposed to temperatures of 130°C for 30 milliseconds during this ablation procedure. The temperature rapidly drops from the skin's surface, yet neither the live tissue nor the nerve endings are impacted. This painless and bloodless procedure

causes a 40–50m diameter section of the brain to be disrupted.

- Testosterone transdermal patch system in young women with spontaneous premature ovarian failure:

In premenopausal women, daily testosterone production is around 300 g, with half coming from the ovaries and half from the adrenal glands. When compared to normal ovulatory women, young women with spontaneous premature ovarian failure (sPOF) may have lower testosterone levels. The Testosterone Transdermal Patch (TTP) was created to mimic the normal ovarian testosterone production rate. In women with sPOF, adding TTP to cyclic E2/MPA treatment resulted in mean free testosterone levels that were close to the upper limit of normal10

- Transdermal patch of oxybutynin used in overactive bladder:

The product is a transdermal patch containing Oxybutynin HCl that is approved in the United States and Europe under the brand names Oxytrol and Kentera. OXYTROL is a thin, flexible, clear patch that is applied twice weekly to the belly, hip, or buttock and delivers oxybutynin in a continuous and regular manner over a three to four day period. OXYTROL provides OAB. Patient's continued effective bladder control while avoiding some of the oral formulation's adverse effects, such as dry mouth and constipation. However, for the majority of patients, these side effects are not bothersome9.

- Nanotechnology gaining hold:

Microneedles are another enhancement that is gaining popularity. This method combines the benefits of a needle and a transdermal patch in one device. The gadgets are dime-sized polymer chunks with hundreds of hollow microneedles ranging in length from 100 to 1,000 micrometres. These tiny needles pierce the top layers of skin, allowing the medication to easily pass through. This technology can be used in conjunction with an electrically controlled micropump that distributes the medicine at predetermined intervals or on demand. These devices, once approved by the FDA, would allow the patient or physician to manage the time and dose of the drug being given. These devices have the ability to precisely deliver medications in the area where particular immune cells reside, allowing these treatments to modulate the immune system.

- Pain treatment:

Transdermal patch technology is frequently used for pain relief. The Duragesic patch is well-known to the majority of readers. There are a slew of others on the market right now. One of these is Lidoderm, a lidocaine 5 percent patch used to treat postherpetic neuralgia. The ETrans fentanyl HCl patch is another promising innovation in pain management. This credit card-sized patch is an active delivery system with a self-contained battery that administers fentanyl HCl, a powerful narcotic, in pulses. This is similar to the use of intravenous self-controlled analgesia systems, which are expensive, inconvenient, and require a lot of nursing care11.

- Absorption enhancers, or chemicals:

that help medications pass through the stratum corneum, have been the subject of extensive investigation. Terpene derivatives, as well as terpenes themselves Some phenols appear to help with transdermal absorption. Linalool, alpha terpineol, and carvacrol, for example, have been examined in combination with haloperidol (a commonly prescribed neuroleptic drug). Although all three improved haloperidol absorption, only linalool elevated it to a therapeutic level. Limonene, menthone, and eugenol were reported to improve tamoxifen transdermal absorption. The polyphenol phloretin improved the absorption of lignocaine. Absorption enhancement research has generally been conducted on excised animal skin (pig or rabbit) or human skin derived from cadavers or plastic surgery procedures[12]

- Technologies and approaches for the future:

Thermal poration is the process of creating water channels through the stratum corneum using pulsed heat. This method has been utilised to administer conventional medications and to extract intestinal fluid glucose from human subjects. 8,13.

- Jet injectors are getting a lot of attention these days, which is leading to better device design for controlled, needle-free injection of medication solutions across the skin and into deeper tissue.
- Morphine has been delivered to humans using this method. A small needle is placed a few millimetres into skin, and drug solution is pumped via the needle into the skin at controlled rates using a microinfusion pump contained within a big patch fastened to skin.
- Several explanations have been proposed throughout the last decade. nonpainful, safe and effective alternative to current intramuscular or subcutaneous vaccination methods
- Altea Therapeutics is currently in clinical development of a transdermal patch designed to address a major unmet need by preventing ‘off’ periods and provide an improved therapeutic option for managing Parkinson’s disease.

Conclusion:

In above study we studied principles, kinetics of Transdermal Permeation. Also, we studied parameters, approaches used, development and recent advances in Transdermal patches.

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