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A COMPREHENSIVE REVIEW ON MATRIX TYPE TRANSDERMAL PATCHES

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ABSTRACT

Transdermal drug delivery system was presented to overcome the difficulties of drug delivery especially oral route. A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. It promotes healing to an injured area of the body. Transdermal drugs are self-contained, discrete dosage form. It also provides controlled release of the drug for extended period of the time. Drug delivery through the skin to achieve a systemic effect without producing any fluctuations in plasma concentration of the drug. This review article covers introduction, outline advantages, disadvantages, skin pathways for transdermal drug delivery systems, various components of transdermal patches, preparation of transdermal patches, factor affecting transdermal patches, evaluation of transdermal system.

KEYWORDS: Transdermal drugs are self-contained, discrete dosage form.

INTRODUCTION

Drug administered in the conventional dosage forms usually produce large range in fluctuations in plasma drug concentrations leading to undesirable toxicity or poor effectiveness. Oral route is most popular route of drug delivery system, but it has some disadvantages including first pass metabolism, drug degradation in gastrointestinal tract due to enzymes and Ph.[1] To overcome these problems and to ensure safety, to improve efficacy of drug as well as patient compliance. The transdermal drug delivery system was developed. In this system medicated adhesive patches are prepared which deliver therapeutically effective amount of drug across the skin when it placed on skin. They are available in different sizes and having more than one ingredient. Once they apply on unbroken skin. They deliver active ingredients into systemic circulation passing via skin barriers. A transdermal patch containing high dose of drug inside which is retained on the skin for prolonged time period, which get enters into blood flow via diffusion process.[2]

Drug can penetrate through skin via three pathways: -

a) Through hair follicles.
b) Through sebaceous glands.
c) Through sweat ducts.

Transdermal drug delivery systems are used in various skin disorders, also in the management of angina pectoris, pains, smoking cessation and neurological disorders such as Parkinson's disease.

Physiology of the Skin

Skin of an average adult body covers a surface of approximately 2 m square and receives about one-third of the blood circulating through the body. Skin contains an uppermost layer, epidermis which has morphologically distinct regions; basal layer, spiny layer, stratum granulosum and upper most stratum corneum, it consists of highly cornified cells embedded in a continuous matrix of lipid membranous sheets.[3] These extracellular membranes are unique in their compositions and are composed of ceramides, cholesterol and free fatty acids. The human skin surface is known to contain, on an average, 10-20 hair follicles and 200-250 sweat ducts on every square centimeters of the skin area, it is one of the most readily accessible organs of the human body.[4]

Skin Pathways for Transdermal Drug Delivery

When drugs are applied on the skin surface, penetration into and through the skin can occur via various routes. Drugs penetrate either via the stratum corneum or via the appendages. During penetration through the stratum corneum, two possible routes can be distinguished, penetration alternating through the corneocytes and the lipid lamellae and penetration along the tortuous pathway along the lipid lamellae.[5] Generally, it is accepted that the predominant route of penetration through the stratum

corneum is the intercellular route. This is mainly caused by the densely cross-linked cornified envelope coating the keratinocytes.

However, transcellular transport for small hydrophilic molecules such as water cannot completely be excluded. The appendage route or shunt route includes either the duct of the eccrine sweat glands or the follicular duct. The content of the eccrine sweat glands is mainly hydrophilic, while the content of the follicular duct is lipophilic. This is mainly due to the sebum excreted into the opening of the follicular duct. It is generally accepted that due to its large surface area, passive skin permeation mainly occurs through intact stratum corneum.[6]

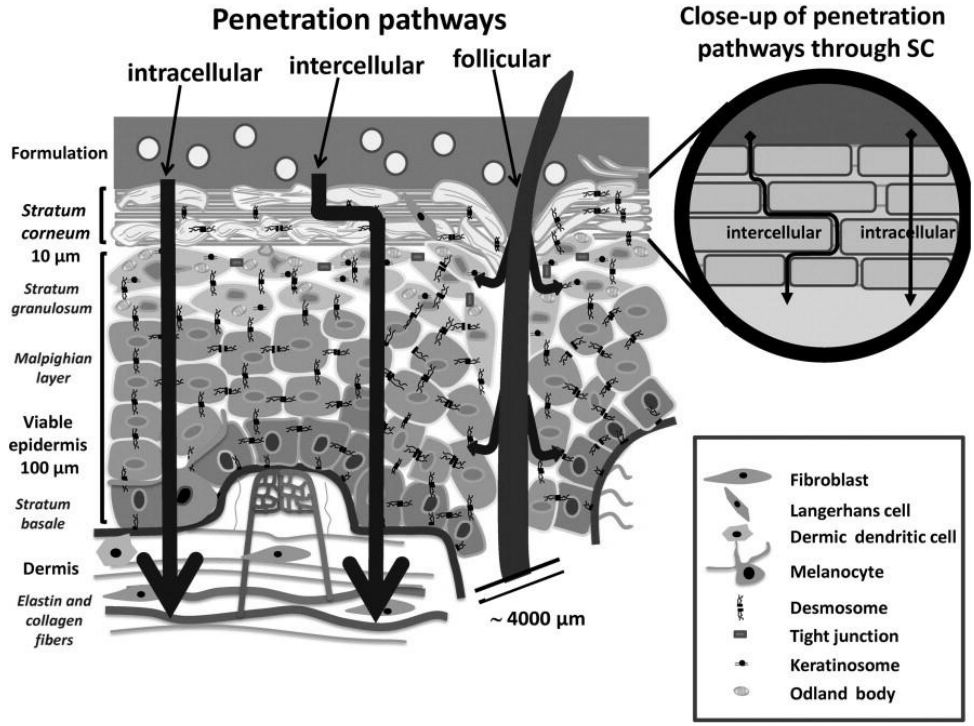

Figure 1: Penetration pathway fro transdermal drug delivery.

Matrix Type Transdermal Drug Delivery System

Matrix system is of two types

- Drug-in-Adhesive System: - For the formation of drug reservoir, the drug dispersed in an adhesive polymer and then spreading the medicated polymer adhesive by solvent casting or by melting the adhesive on to n impervious backing layer.[7]
- Matrix-dispersion System: - In this system the drug is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. And this containing polymer along with drug is fixed onto an occlusive base plate in a compartment fabricated from a drug-impermeable backing layer. In this system the adhesive is spread along the circumferences instead of applying on the face of the drug reservoir to form a strip of adhesive rim.[8]

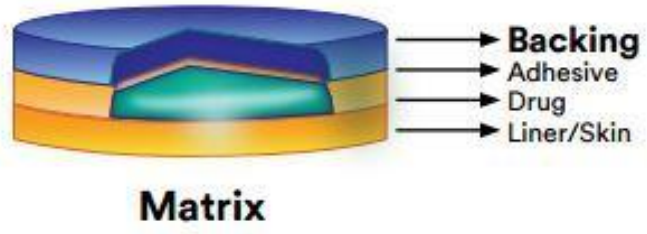

Figure 2: Components of transdermal drug delivery system.

Components of Transdermal Drug Delivery System

- ✓ Polymer matrix
- ✓ Drug
- ✓ Permeation enhancer
- ✓ Pressure sensitive adhesive
- ✓ Backing laminate
- ✓ Release liner
- ✓ Other excipients like plasticizers and solvents

Polymer matrix: the polymer matrix controls the release of the drug from the device. The following criteria should be satisfied for a polymer to be used in a Transdermal system. Possible useful polymers for Transdermal devices are shown in table 1.

Table 1: Polymers used in Transdermal patches.

Natural Polymers	Synthetic elastomers	Synthetic polymers
Cellulose dérivatives, Gélatine, Waxes, proteins, Gums, Natural rubber, starch.	Polybutadiene, Hydrin rubber, polysiloxane, silicone rubber, Nitrile, Acrylonitrile, neoprene.	Polyethylene, polypropylene, epoxy, polyurea, polymethyl methacrylate.

Drug: some of ideal properties of drug and some other factors to be consider during preparation of transdermal patches are as follows:

Table 2: Ideal properties of drugs.

S.no	Parameter	Properties
1	Dose	Should be low in Wt. (LT 20mg/day)
2	Half-life	10/less (hrs).
3	Molecular weight	<400da.
4	Skin permeability coefficient	>0.5*10-3cm/hr
5	Skin reaction	Non-irritating, non sensitizing
6	Oral bioavailability	low

Table 3: Factors affecting.

Physicochemical	Pharmacokinetic	Biological
Solubility	Half-life	Skin toxicity
Crystallinity	Volume of distribution	Site of application
Molecular weight	Total body clearance	Allergic Reaction
Polarity	Therapeutic plasma conc.	Skin metabolism
Melting point	Bioavailability factor	

Permeation enhancers: the chemical compounds hat enhance the permeability of stratum corneum so as to attain therapeutic levels of the drug candidate. They improve the permeability by interacting with stratum corneum.[9]

Ideal properties of permeation enhancers:

1. They should be non-irritating, non-toxic and non-allergic.
2. They should not bind to receptor site i.e. not showing any pharmacological activity.
3. They should be cosmetically acceptable with an appropriate skin feel.

Pressure sensitivity Adhesive: it helps to increase the adherence of transdermal patch to the skin surface. It can easily remove from the surface without leaving a residue on it.[10]

1. Polyacrylates
2. Polyisobutylene
3. Silicon based adhesive

Backing laminate: it is a supportive material which is impermeable to drugs and also to permeation enhancers. They should chemically compatible with the drug, enhancer, adhesive and other excipients. Ex: vinyl, polyethylene and polyester films.[11]

Release liner: This is the primary packaging material that can protect the patch during application. It is made up of base layer which may be

Non-occlusive (e.g. Paper fabric)
Or
Occlusive (e.g. polyéthylène, Polyvinylchloride)

It is made up of Silicon or Teflon. Release liner should be chemically inert and it should be permeable to drug, penetration enhancers and water.[12]

Other excipients like plasticizers and solvents

Solvents: Chloroform, Methanol, Acetone, Isopropanol and dichloromethane.
Plasticizers: Dibutylphthalide,t riethylcitrate, polyethylene glycol and propylene glycol.

Preparation of Transdermal Patches

Transdermal drug delivery patches can be prepared by various methods:

Mercury Substrate Method: In this method required amount of drug is dissolved in predetermined amount of polymer solution along with plasticizer. The above solution is to be stirred for some time to produce a homogeneous dispersion and it is kept aside until air

bobbles removed completely and then poured into a glass ring which is placed over the mercury surface in a glass petri dish. The rate of evaporation of the solvent is controlled by placing an inverted funnel over the petri dish. The dried films are to be stored in a desiccator.[13]

Circular Teflon Mould Method

Solutions containing polymers in various ratios are used in an organic solvent. Calculated amount of drug is dissolved in half the quantity of some organic solvent. Plasticizer added into drug polymer solution. The total contents are to be stirred and then poured into a circular Teflon mould. And rate of solvent vaporization controlled with placing inverted glass funnel on Teflon mould. The solvent is allowed to evaporate for 24 hrs. the dried films are to be stored in a desiccator.[14]

Glass Substrate Method: the polymeric solutions are kept a side for swelling then required quantity of plasticizer and drug solution are added and stirred for 10 min. further, it is set a side for some time to exclude any entrapped air and is then poured in a clean and dry anumbra petri plate. The rate of solvent evaporation is controlled by inverting a glass funnel over the petri plate. After over night, the dried films are taken out and stored in a desiccator.

By Using IPM Membranes Method: in this method drug is dispersed in a mixture of water and propylene glycol containing carbomer 940 polymers and stirred for 12 hrs. in magnetic stirrer. The dispersion is to be neutralized and made viscous by the addition of triethanolamine. Buffer Ph 7.4 can be used in order to obtain solution gel, if the drug solubility in aqueous solution is very poor. The formed gel will be incorporated in the IPM membrane.[15]

By Using EVAC Membranes Method: In order to prepare the target transdermal therapeutic system, 1% Carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membranes can be used as rate control membranes. If the drug is not soluble in water, propylene glycol is used for the preparation of gel. Drug is dissolved in propylene glycol; Carbopol resin will be added to the above solution and neutralized by using 5% w/w sodium hydroxide solution. The drug is placed on a sheet of backing layer covering the specified area. A rate controlling membrane will be placed over the gel and the edges will be sealed by heat to obtain a leak proof device.[16]

Aluminium Backed Adhesive Film Method: Transdermal drug delivery system may produce unstable matrices if the loading dose is greater than 10 mg. aluminium backed adhesive film method is a suitable one. For preparation of same, chloroform is choice of solvent, because most of the drugs as well as adhesive are soluble in chloroform. The drug is dissolved in chloroform and adhesive material will be added to the drug solution and dissolved. A custom-made aluminium former is lined with aluminium foil and the ends blanked off with tightly fitting cork blocks.[17]

Asymmetric TPX membrane method: A protype patch can be fabricated by a heat sealable polyester film with concave of 1 cm diameter used as the backing membrane, covered by a TPX (poly 4- methyl-1-pentene) asymmetric membrane, and sealed by an adhesive.

Factor Affecting Transdermal Patches

There are various factors which affects the action of transdermal patches. These are given below:

1. **Physicochemical properties**
- Partition coefficient
- Molecular size
- Solubility
- Melting point
- Ionization

2. **Physiological and pathological conditions of skin**
- Reservoir effect of horny layer
- Lipid film
- Skin temperature
- Regional variation
- Pathological injuries to the skin
- Skin hydration
- Cutaneous self-metabolism
- Skin barrier properties in the neonate and young infant
- Skin barrier properties in aged skin
- Race
- Body site
- Penetration enhancers used

Advantages and Disadvantages of Transdermal Patches

Advantages

a) First pass metabolisms of drug get avoided.
b) Gastrointestinal incompatibilities get avoided.
c) Self-medication is possible
d) Duration of action gets extended and predictable.
e) Unwanted side effects get minimized.
f) Drug plasma concentration getsmaintained.
g) Numbers of doses get reduces which improve patient compliances.

Disadvantages

1. Chances of allergic reactions at the site of application like- itching, rashes, local edema etc.
2. Larger molecular size of drug (1000) creates difficulty in absorption.
3. Barrier function of skin varies from site to site on the same or different person.
4. Drug with hydrophilic character is less suitable as compare to drug with lipophilic character because of their low permeability.[18]

Evaluation Test of Transdermal Patch

- **Drug excipients interaction studies:** the drug excipients should be compatible to produce a stable product, and it is mandatory to detect any possible physical and chemical interaction. Interaction studies are commonly carried out using thermal analysis, FT-IR studies, UV and chromatographic techniques.[19]
- **Drug content:** A specified area of the patch is to be dissolved in a suitable solvent in specific volume.
- **Weight uniformity:** the prepared patches are to be dried at 60 degree Celsius for 4 hrs. before testing. A specified area of the patch is cut into different parts and weigh in digital balance.
- **Thickness of the patch:** thickness of the drug loaded patch is measured in different points by using a digital micrometre.[20]
- **Percentage moisture uptake:** the weight films are to be kept in desiccator at room temperature for 24 hrs. containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 hrs. the film are to be reweighed and determine the moisture uptake.
- **Moisture loss:** the prepared films are to be weighed individually and to be kept in a desiccator containing calcium chloride at 40 degree Celsius. After 24 hrs. the films are reweighed and determine the percentage of moisture loss.
- **Skin irritation study:** skin irritation and sensitization testing can be performed on healthy rabbits.
- **In vitro drug release studies:** the paddle over disc method can be employed for assessment of the release of the drug from the prepared patches.[21]
- **In vitro skin permeation studies:** an in vitro permeation study can be carried out by using diffusion cell.[22]
- **In vivo studies:** in vivo studies are carried out on animal models and human volunteers.
- Animal models: the most common animal species are used for evaluating transdermal drug delivery system are mouse, hairless rat, hairless dog, monkey, rabbit, guinea pig etc.[23]
- **Human volunteers:** the final stage of the development of a transdermal device involves collection of pharmacokinetic and pharmacodynamic data following application of the patch to human volunteers. Clinical trials have been conducted to assess the efficacy, risk involved, side effects, patient compliances etc.[24]

CONCLUSION

Transdermal drug delivery is a painless, convenient, and potentially effective way to deliver regular doses of many medications. Wide range of drugs can be delivered improved drug uptake, minimal complications and side effects, low cost and easy to use. Transdermal delivery of a drug product which is currently approved as oral dosage form, allows for the avoidance of first pass metabolism. However, the transdermal technologies have limitations due to the relatively impermeable thick of outer stratum corneum layer. Researchers are trying to overcome this hurdle of poor permeability by physical and chemical means.

REFERENCES

1. Panner Selvam R, Anoop Kumar Singh, Sivakumar T, Transdermal drug delivery systems for antihypertensive drugs - A review, IJPBR, 2010; 1(1): 1-8.
2. Gurpınar SS, Devrim B, Eryılmaz M. *In-vitro* antibacterial activity of *lactobacilli* metabolites loaded hydrogel formulations against *pseudomonas aeruginosa*. Universal Journal of Pharmaceutical Research, 2019; 4(4): 10-12.
3. Kakkar A, 2.P and Ajay Gupta, Gelatin Based Transdermal Therapeutic System, Indian Drugs, 1991; 29(7): 308-315.
4. Neelam Chauhan, Kapil Kumar, Navin Chandra Pant. An updated review on transfersomes: a novel vesicular system for transdermal drug delivery. Universal Journal of Pharmaceutical Research, 2017; 2(4): 49-52.
5. Chowdary K.P.R and Naidu R.A.S, Transdermal Drug Delivery, A Review of Current Status, Indian Drugs, 1995; 32(9): 414- 422.
6. Fatima AA, Chukwuka UK. Development and *in-vitro* evaluation of matrix-type transdermal patches of losartan potassium. Universal Journal of Pharmaceutical Research, 2017; 2(2): 39-43.
7. Divyesh Patel, Nirav Patel, Transdermal Drug Delivery System Review, International Journal of Biopharmaceutical and Toxicological Research, 2011; 1(1): 61-80.
8. YieW, Chien, Novel Drug Delivery Systems, 2nd ed, M. Dekker, 2005; 50: 301-380.
9. EseldinKeleb, Rakesh Kumar Sharma, Transdermal Drug Delivery System-Design and Evaluation, International Journal of Advances in Pharmaceutical Sciences, 2010; 1(3): 201-211.
10. Ugochukwu AE, Nnedimkpa OJ, Rita NO. Preparation and characterization of Tolterodine tartrate proniosomes, Universal Journal of Pharmaceutical Research, 2017; 2(2): 22-25.
11. Ankush I, Shembale, Useful Permeation Enhancers for Transdermal Drug Delivery A Review, IJPRD, 2010; 5: 1-6.
12. Saifullahi Umar, Moh Kingsley Onyekachi. Development and evaluation of transdermal gel of Lornoxicam. Universal Journal of Pharmaceutical Research, 2017; 2(1): 17-20.
13. Hadgraft J.W, and Somers G.F, Review Article Percutaneous absorption, International Journal of Pharmaceutics, 2005; 305: 2-12.
14. Gilbert S, Banker, Christopher T, Rhodes, Modern Pharmaceutics, 2nd Ed, Revised and Expanded, 40: 263-298,
15. Jain N. K, Controlled and Novel Drug Delivery, 1997; 100-115.

16. SwarnlataSonl and Vinod K, Dixit, Transdermal Penetration Enhancers, Categorization, Indian Drugs, 1992; 29(11): 465- 471.
17. Elsaied Hamada Elsaied, Hamdy Mohamed Dawaba, Elsherbini Ahmed Ibrahim, Mohsen Ibrahim Afouna. Investigation of proniosomes gel as a promising carrier for transdermal delivery of Glimepiride. Universal Journal of Pharmaceutical Research, 2016; 1(2): 1-18.
18. Tanu Bhargava, Current trends in NDDS with special reference to NSAIDS, International Journal of Pharma and Bio Sciences, 2011; 2: 92-114.
19. Dingwoke John Emeka Francis. Development and evaluation of matrix type transdermal patches of pioglitazone hydrochloride. Universal Journal of Pharmaceutical Research, 2016; 1(1): 31-37.
20. Lyn Margetts, and Richard Sawyer, Transdermal Drug Delivery: Principles And opioid Therapy, Continuing Education in Anaesthesia, Critical Care & Pain, 2007; 7(5): 171-176.
21. Nikhil Sharma, Geta Agarwal, Rana A.C, A Review Transdermal Drug Delivery System a tool for Novel Drug Delivery System, IJDDR, 2011; 3(3): 70.
22. Ejiogu Deborah Chioma. Formulation and evaluation of etodolac niosomes by modified ether injection technique. Universal Journal of Pharmaceutical Research, 2016; 1(1): 1-6.
23. Mohamed Aqil, Yasmin Sultana and Asgar Ali, Matrix Type Transdermal Drug Delivery Systems of Metoprolol Tartrate, Invitro Characterization, Acta Pharm, 2003; 53: 119-125.