

# A Novel Transdermal Drug Delivery System and Its Applications in Present Scenario

B. Bhuvana, S. Nagalakshmi\*, S. Shanmuganathan

Department of Pharmaceutics, Faculty of Pharmacy, Sri Ramachandra University.

\*Corresponding author: E-Mail: nagalakshminpharm@gmail.com

## ABSTRACT

The major purpose of transdermal drug delivery system (TDDS) is to overcome the difficulties through oral route. The major advantages of TDDS are improved bioavailability with controlled release of drug, reduced side effects and bypass first pass metabolism. In the last two decades, TDDS has developed as a verified technology which shows more clinical benefits over other dosage forms, since it is controlled and releases predetermined amount of drug into the site; also it helps to retain the concentration of blood in a steady state level. This review article describes the polymers suitable to be formulated as transdermal system, advantages, disadvantages and applications of transdermal patches.

**KEY WORDS:** Transdermal Drug Delivery Systems, Transdermal Patches, First Pass Metabolism, Controlled Drug Release, Steady State Blood Concentration.

## 1. INTRODUCTION

Many substances are applied as cosmetics and therapeutic agents on human skin from their beginning of life on the earth. However the skin has become the route for long term delivery on twentieth century (Reddy, 2014). At present scenario, about 74% of drugs are administered orally and are found to have some limitations like first pass metabolism, low bioavailability etc. (Patel, 2012). In pharmaceutical industry improving a controlled dosage form has become increasingly significant. Therefore different types of NDDS (novel drug delivery system) such as controlled release systems, TDS (transdermal delivery system), transmucosal delivery systems etc. has been urbanized (Kaur, 2015). From the above mentioned technique TDDS is most broadly accepted and appealing as valuable technique for drug release in a restricted way into the human body (Reddy, 2014). TDDS documented itself as an essential part of NDDS, with the formation of present time of pharmaceutical dosage forms. Though TDDS is an expensive substitute to conventional delivery system, it is being accepted due to their limited advantages. Transdermal drug delivery system includes many possible advantages and they are discussed later in this article (Patel, 2012). In transdermal drug delivery device either active or passive way of administering medication can be achieved. The drug to be distributed across the skin barrier can be attained through this device. The principle behind TDDS is that a drug is administered in a comparatively low amount at the surrounded area by a patch or other system, which retains on the surface of skin for prolonged period of time. Throughout the distribution course, the drug enters directly through the skin into the blood stream and hence a higher concentration is obtained in blood. The drug keeps circulating in the human blood for a longer episode of time retaining the unchanging drug's concentration in the blood flow (Ancel, 2002; Prajapati, 2011).

**Definition:** A Transdermal patch is defined as the adhesive patch which contains medicament and is kept above the surface of skin in order to distribute a definite amount of medicament via the surface of skin with a specified rate of drug release to reach the systemic circulation. The marketed formulations of TDS patches, which is mainly based on principle of semi permeable membrane (Patel, 2012; Prajapati, 2011).

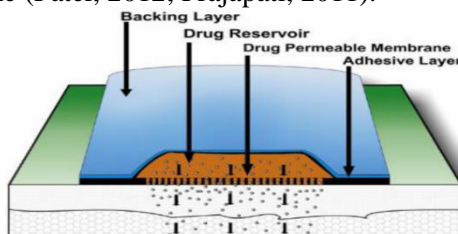


Figure.1. Transdermal patch showing its different components

### Classification (Richa Sachen, 2013):

**Single layer drug in adhesive:** In this classification, the excipients and the drugs are compounded with skin adhesive which provide a better mean of formulation acting as a single layer. The release of drug takes place via diffusion phenomenon.

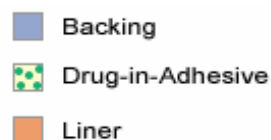
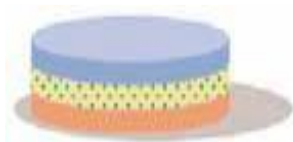


Figure.2, Single layer drug in adhesive patch and its different components

The rate of drug release is given as

$$\frac{dQ}{dT} = \frac{Cr}{\frac{1}{P_m} + \frac{1}{P_a}}$$

Where,  $P_a$  = permeability coefficient of adhesive layer;  $C_r$  = the concentration of drug in the compartment containing reservoir;  $P_m$  = rate controlling membrane's permeability coefficient.

**Multi drug layer in adhesive:** Here, the excipients and drug integrated with bonding agent. They are divided by a membrane of single layer. The discharge of drug occurs via diffusion phenomenon.



**Figure.3. Multi-layer drug in adhesive patch and its different components**

The rate of drug release is given as below:

$$\frac{dQ}{dT} = \frac{K_a}{r} \cdot \frac{D_a}{h_a} C_r$$

Where,  $\frac{K_a}{r}$  = drug's partition coefficient between the reservoir layer and bonding agent layer.

**Drug reservoir in adhesive:** Here, addition of liquid compartment consists of drug solution/suspension in between the backing layer and the semi permeable membrane backed by layer of adhesive type and layer of release as shown in the below figure.



**Figure.4. Drug reservoir in adhesive patch and its different components**

The drug release rate is expressed as below:

$$\frac{dQ}{dT} = \frac{K_a}{r} \cdot \frac{D_a}{h_a(t)} A(h_a)$$

Where,  $H_a$  = Adhesive layer thickness;  $A$  = diffusion path thickness.

**Drug matrix in adhesive:** In this system the portion of adhesive is intended by addition of matrix of semisolid part having drug in suspension or solution form which is in contact with the release layer.



**Figure.5. Single layer drug in adhesive patch with its different components**

The drug release rate is governed as below:

$$\frac{dQ}{dT} = \frac{AC_p D_p}{2t} \frac{1}{2}$$

Where,  $A$  = the early loading dose of the drug detached in the matrix containing polymer;  $C_p$  = drug's solubility;  $D$  = polymer drug diffusion.

**Basic Components of Transdermal Drug Delivery Systems (Bhowmik, 2010):** The basic components of TDDS include:

- Polymer matrix or matrices
- Drug
- Permeation enhancers
- Other excipients

**Polymer Matrix:** From the device the drug release is restricted by the polymer.

Probable helpful polymers for TDDS are: Polymers	Example
Natural polymers	Zein, Shellac, Proteins, Waxes, Starch, etc.,
Synthetic elastomers	Polybutadiene, Siliconer Rubber.

**Drug:** Drug must be selected with huge concern for productively rising a TDDS. The physicochemical property of a drug is given as below:

**Physicochemical properties:**

- The drugs molecular weight should not be more than 1000 Daltons.
- It must be compatible for phases like hydrophilic and lipophilic phases.
- The M.P must be low for the drug.
- Drug should possess short half-life.
- It must be effective and should be less-irritant.

**Permeation enhancers:** Permeation enhancers should support permeability of the skin by varying the obstruction to the flux of a preferred penetrant. The classification of permeation enhancers are below

**Solvents:** These compounds enhance diffusion probably by swallowing the fluidizing lipids and/or by polar pathway. The examples are given as below:

**Table.1. Example of different solvents**

S.No	Examples
1	Water alcohols like methanol and ethanol
2	Alkyl methyl sulfoxides like dimethyl sulfoxide
3	Alkyl homologues of methyl sulfoxide dimethylacetamide
4	Pyrrolidones like 2-pyrrolidone
5	N-methyl

**Surfactants:** surfactants are the compounds that are anticipated to improve polar pathway transport, particularly of hydrophilic drugs. The capability of these compounds is to modify diffusion is a purpose of head of polar group and chain length of hydrocarbon group. The examples include dioctyl sulphosuccinate and SLS (sodium lauryl sulphate).

**Miscellaneous chemicals:** some of the miscellaneous chemical compounds are listed as below:

**Table.2. Example of different miscellaneous chemicals**

S.no.	Compounds
1	Urea
2	Hydrating and kerolytic agent
3	N,N-dimethyl-m-tuloamide
4	Anticholinergic afents
5	Eucalyptol
6	di-o-methyl- $\beta$ -cyclodextrin
7	Soyabean

**Other excipients:**

**Adhesives:** The adhesives used in the formulation should possess the following criteria:

- It should be easily removed and should hold on to the surface of the skin forcefully.
- No residue should be on the skin.
- It should be non-irritant.

**Backing membrane:** They are more stretchable and they are attached well to the reservoir of the drug.

**Advantages** (Latheeshjlal, Patel, 2012):

- TDDS avoids the first pass effect for example transdermal nitroglycerine, when taken orally it is rapidly metabolized by the liver so it can be administered by TDDS.
- For some patient they cannot endure oral dosage forms, in such case TDDS can be used.
- In TDDS self administration is easy.
- Through this system improved bioavailability can be attained.
- This system has some additional advantages like enhanced patient conformity and comfort via non-invasive, effortless and easy application.
- Dosing frequency is reduced due to its longer period of action.
- Steady state plasma level concentration is attained.
- It is of great benefit in patients who are disgusted or comatose.

**Disadvantages** (Nitin Saini, 2014; Patel Harunusman, 2012):

- There are many possibilities for formation of Erythema, Itching and Local Edema due to the drug or other excipients that are used in the formulation of patch.
- Hydrophilic drugs may not achieve the therapeutic level as it permeate through the skin too slowly.
- Long time stay is difficult
- For some drugs it is not comfortable for example scopolamine transdermal patch which is placed behind the ear.
- Due to the type of the patch and environmental conditions the linkage may vary.

- It is not suitable for high drug doses i.e. more than 10mg/day.

**Applications** (Chetan Ghulaxe, 2015; Jain, 1997):

- Duragesic (chemically fentanyl) and BuTrans (chemically Buprenorphine) medications are used to provide immediate relief for severe pain.
- Nicotine patch which delivers the drug in steady state doses to help with termination of smoking of tobacco.
- In treatment of angina in lieu of sublingual pills Nitroglycerine patches are given.
- Patches containing estrogens are prescribed for menopausal symptoms as well as post menopausal osteoporosis.
- The first TDDS agent for an antidepressant is transdermal form of the MAOI selegiline.
- Clonidine which is an anti-hypertensive drug is used in TDDS form.
- Transdermal delivery agent for the Attention Deficit hyperactivity disorder.

**2. CONCLUSION**

This review article gives important details of TDDS, its classification, its basic components, and its application. Many drugs have been formulated in TDDS form, for hormonal therapy, wide range of analgesics, drugs for heart diseases, for avoiding GI effects and first pass metabolism. Dermal patches are the most common form of transdermal delivery of drugs. 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**

Ancel H.C and Popovich N.G, Pharmaceutical Dosage Forms and Drug Delivery Systems, Seventh edition, Lipincott Williams and Willikins publication, 2, 2002, 234.

Bhowmik D, Recent advances in transdermal drug delivery system, International Journal of PharmTech Research, 2 (1), 2010, 68–77.

Chetan Ghulaxe & Rameshwar Verma, A review on transdermal drug delivery system, The Pharma Innovation Journal, 4 (1), 2015, 37-43.

Chien YW, Novel drug delivery systems, Drugs and the Pharmaceutical Sciences, Marcel Dekker, New York, 50, 1992, 797.

Jain NK, Controlled and Novel Drug Delivery, CBS Publishers and Distributors, New Delhi, 107, 2002.

Jain NK, Controlled and novel drug delivery, Ist edition, CBS publishers and distributors, New Delhi, 1997.

Kaur D & Singh R, A Novel Approach, Transdermal Gel, 4 (10), 2015, 41–50.

Latheeshj Lal L, Phanitejaswini P, Soujanya Y, Swapna U, Sarika V, Moulika G, Transdermal Drug Delivery Systems, An Overview, IJPRIF, 3 (4), 2140-2148.

Nitin Saini & Anshul Bajaj, Recent Trend on Transdermal Drug Delivery System and Advancements in Drug Delivery Through Skin, A Review, International Journal of Research in Pharmaceutical and Biosciences, 2014.

Patel D, Transdermal Drug Delivery System, A Review, Online, 1 (4), 2012, 78–87.

Patel Harunusman, Patel Upendra Daslaniya, Patel, Bhimani Bhavin Daslaniya, Patel Ghanshyam, Bhimani, Dhiren, Transdermal drug delivery system as prominent, Dosage forms for the highly lipophilic drug, 1 (3), 2012, 42-65.

Prajapati S.T, Patel C.G & Patel C.N, Formulation and Evaluation of Transdermal Patch of Repaglinide, ISRN Pharmaceutics, 2011, 1–9.

Premjeet Sandhu, Bilandi Ajay, Sahil Kataria and Akanksha Middha, Transdermal drug delivery system (patches), Applications in present scenario, 1 (4), 2011.

Reddy Y.K, Reddy D.M & Kumar M.A, Transdermal Drug Delivery System, A Review, Indian Journal of Research in Pharmacy and Biotechnology, 2 (2), 2014, 1094-1103.

Richa Sachen & Meenakshi Bajpai, Transdermal Drug Delivery System, A Review, International Journal of Research and Development in Pharmacy and Life Sciences, 3 (1), 2013, 748-765.