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# Transdermal Drug Delivery: Innovations, Challenges, and Future Directions

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## Abstract

Transdermal drug delivery systems (TDDS) are increasingly utilized to administer drugs across the skin for systemic effects. This review discusses the skin structure and the mechanism of drug penetration through different skin layers, emphasizing the physicochemical properties required for effective transdermal permeation. We explore various types of TDDS, such as matrix, reservoir, and drug-in-adhesive systems, detailing their composition, operation, and the role of excipients like permeation enhancers. The kinetics of drug permeation and the impact of chemical enhancers on this process are analyzed. Additionally, the design and evaluation methods of TDDS, including physicochemical stability, in vitro, and in vivo performance assessments, are extensively reviewed. By enhancing the understanding of TDDS components and mechanisms, this article contributes to the development of more effective transdermal therapeutic solutions.

**Keywords:** Transdermal Drug Delivery, Permeation Enhancers, Drug Permeation Kinetics, TDDS, Chemical Penetration Enhancers

## INTRODUCTION

Transdermal drug delivery system are topicaly administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate.[1]

### A BRIEF REVIEW OF SKIN STRUCTURE

The skin can be considered to have four distinct layers of tissues;
1. Non-viable epidermis (stratum corneum)
2. Viable epidermis
3. Viable dermis
4. Subcutaneous connective tissue (hypodermis)

## NON-VIABLE EPIDERMIS (STRATUM CORNEUM)

Stratum corneum is the outer most layer of skin, which is the actual physical barrier to most substance that come in contact with the skin. The stratum corneum is 10 to 20 cell layer thick over most of the body. Each cell is a flat, plate-like structure - 34-44 µm long, 25-36 µm wide, 0.5 to 0.20 µm thick - with asurface area of 750 to 1200 µm stocked up to each other in brick like fashion. Stratum corneum consist of lipid (5-15%) including phospholipids, glycosphingolipid, cholesterol sulfate and neutral lipid, protein (75-85%) which is mainly keratin.

## VIABLE EPIDERMIS

This layer of the skin resides between the stratum corneum and the dermis and has a thickness ranging from 50-100 µm. The structure of the cells in the viable epidermis are physiochemically similar to other living tissues. Cells are held together by tonofibrils. The density of this region is not much different than water. The water content is about 90%.

## DERMIS

Just beneath the viable epidermis is the dermis. It is a structural fibrin and very few cells are like it can be found histologically in normal tissue. Dermis thickness range from 2000 to 3000µm and consists of a matrix of loose connective tissue composed of fibrous protein embedded in an amphorphose ground substance.

## SUBCUTANEOUS CONNECTIVE TISSUE

The subcutaneous tissue is composed of loose textured, white, fibrous connective tissue containing blood and lymph vessels, secretary pores of the sweat gland and cutaneous nerves. Drug permeating through the skin enter the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug.

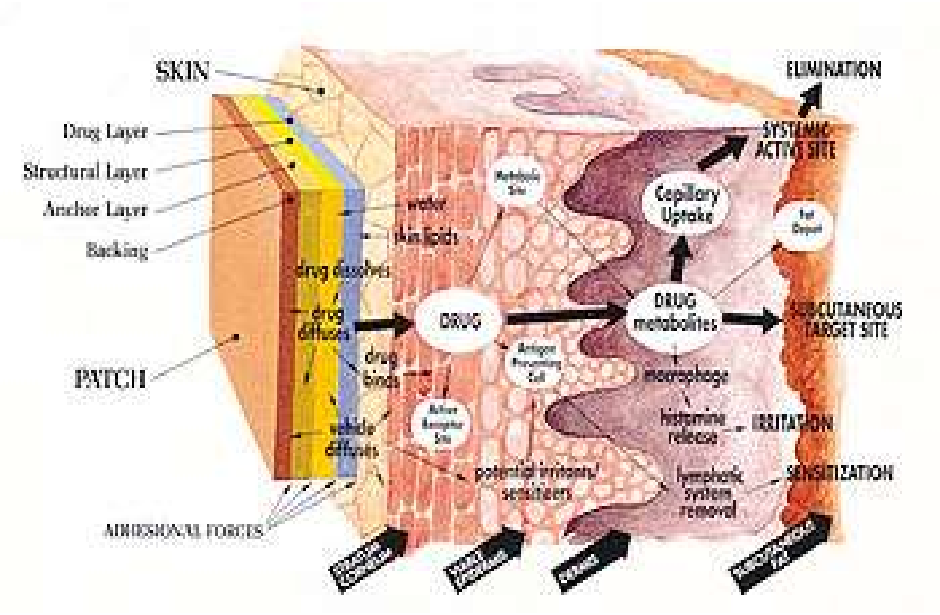


**Fig 1: Transport processes in transdermal drug delivery**

## ADVANTAGES OVER CONTROLLED RELEASE FORMULATIONS[3]

- Drugs with very short half lives Eg. Nitroglycerine when administered as transdermal patches, release medicaments at a constant rate for a time period more than that obtainable with oral formulations.
- Drugs with narrow therapeutic indices can be safely administered since better control of release is possible.
- The noninvasive nature of these systems permits easy removal and termination of drug action in situations of toxicity.

- ❖ Problems encountered with oral administration like degradation, gastric irritation, first pass effect, etc. are avoided.

## PATHWAY OF TRANSDERMAL PERMEATION[4]

Permeation can occur by diffusion via:
1. Transdermal permeation, through the stratum corneum.
2. Intercellular permeation, through the stratum corneum.
3. Transappendaged permeation, via the hair follicle, sebaceous and sweat glands.

Most molecules penetrate through skin via intercellular microroute and therefore many enhancing techniques aim to disrupt or bypass its elegant molecular architecture

## KINETICS OF TRANSDERMAL PERMEATION [5]

Skin permeation kinetics is vital to the successful development of transdermal therapeutic systems. Transdermal permeation of a drug involves the following steps:

1. Sorption by stratum corneum.
2. Penetration of drug through viable epidermis.
3. Uptake of the drug by the capillary network in the dermal papillary layer.

The permeation can be possible only if the drug possesses certain physiochemical properties. The rate of permeation across the skin is given by:

$$\frac{dQ}{dt} = P_s ( C_d - C_r ) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where $C_d$ and $C_r$ are the concentration of the skin penetrant in the donor compartment i.e. on the surface of stratum corneum and in the receptor compartment i.e. body respectively. Ps is the overall permeability coefficient of the skin tissue to the penetrant. This permeability coefficient is given by the relationship:

$$K_s P_s = \frac{D_{ss}}{h_s}$$

where $K_s$ is the partition coefficient for the interfacial partitioning of the penetrant molecule from a solution medium or a transdermal therapeutic system on to the stratum corneum, $D_{ss}$ is the apparent diffusivity for the steady state diffusion of the penetrant molecule through a thickness of skin tissues and $h_s$ is the overall thickness of skin tissues. As $K_s$ ,$D_{ss}$ and $h_s$ are constant under given conditions the permeability coefficient Ps for a skin penetrant can be considered to be constant. From equation (1) it is clear that a constant rate of drug permeation can be obtained only when $C_d >> C_r$ i.e. the drug concentration at the surface of the stratum corneum $C_d$ is consistently and substantially greater than the drug concentration in the body $C_r$. The equation becomes:

$$\frac{dQ}{dt} = P_s C_d$$

And the rate of skin permeation is constant provided the magnitude of $C_d$ remains fairly constant throughout the course of skin permeation. For keeping $C_d$ constant the drug should be released from the device at a rate $R_r$ i.e. either constant or greater than the rate of skin uptake $R_a$
i.e $R_r >> R_a$ .

Since $R_r >> R_a$ , the drug concentration on the skin surface $C_d$ is maintained at a level equal to or greater than the equilibrium solubility of the drug in the stratum corneum $C_s$

.i.e. $C_d >> C_s$. Therefore a maximum rate of skin permeation is obtained and is given by the equation:

$(dQ/dt)_m = P_s C_s$
From the above equation the maximum rate of skin permeation depends upon the skin permeability coefficient $P_s$ and is equilibrium solubility in the stratum corneum $C_s$. Thus skin permeation appears to be stratum corneum limited

## BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEMS

The components of transdermal devices include:

1. Polymer matrix or matrices.
2. The drug
3. Permeation enhancers
4. Other excipients

## POLYMER MATRIX

The Polymer controls the release of the drug from the device.

## NATURAL POLYMERS[5]

e.g. Cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.

## SYNTHETIC ELASTOMERS

e.g. Polybutadieine, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrenebutadieine rubber, Neoprene etc.

## SYNTHETIC POLYMERS

e.g. Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinylpyrrolidone, Polymethylmethacrylate, Epoxy etc.

## DRUG

For successfully developing a transdermal drug delivery system, the drug should be chosen with great care

## PHYSICOCHEMICAL PROPERTIES

1. The drug should have a molecular weight less than approximately 1000 daltons.
2. The drug should have affinity for both – lipophilic and hydrophilic phases. Extreme partitioning characteristics are not conducive to successful drug delivery via the skin.
3. The drug should have low melting point.

Along with these properties the drug should be potent, having short half life and be non irritating.

## PERMEATION ENHANCERS

These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant.

## SOLVENTS

These compounds increase penetration possibly by swallowing the polar pathway and/or by fluidizing lipids. Examples include water alcohols – methanol and ethanol; alkyl methyl sulfoxides – dimethyl sulfoxide, alkyl homologs of methyl sulfoxide dimethyl acetamide and dimethyl formamide ; pyrrolidones – 2 pyrrolidone, N-methyl, 2-purrolidone; laurocapram (Azone), miscellaneous solvents – propylene glycol, glycerol, silicone fluids, isopropyl palmitate.

## SURFACTANTS

These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs.The ability of a surfactant to alter penetration is a function of the polar head group and the hydrocarbon chain length.

Anionic Surfactants: e.g. Dioctyl sulphosuccinate, Sodium lauryl sulphate, Decodecylmethyl sulphoxide etc.
Nonionic Surfactants: e.g. Pluronic F127, Pluronic F68, etc.
Bile Salts: e.g. Sodium ms taurocholate, Sodium deoxycholate,
Sodium tauroglycocholate.
Binary system: These systems apparently open up the heterogeneous multilaminate pathway as well as the continuous pathways.e.g. Propylene glycol-oleic acid and 1, 4-butane diol-linoleic acid.

## MISCELLANEOUS CHEMICALS

These include urea, a hydrating and keratolytic agent; N, N-dimethyl-m-toluamide; calcium thioglycolate; anticholinergic agents.Some potential permeation enhancers eucalyptol, di-o-methyl-ß-cyclodextrin and soyabean casein.

## OTHER EXCIPIENTS[4,6,7,8]

## ADHESIVES

The fastening of all transdermal devices to the skin done by using a pressure sensitive adhesive which can be positioned on the face of the device or in the back of the device and extending peripherally. Both adhesive systems should fulfill the following criteria
(i)Should adhere to the skin aggressively, should be easily removed.
(ii)Should not leave an unwashable residue on the skin.
(iii) Should not irritate or sensitize the skin.
The face adhesive system should also fulfill the following criteria.
(i)Physical and chemical compatibility with the drug, excipients and enhancers of the device of which it is a part.
(ii) Permeation of drug should not be affected.
(iii) The delivery of simple or blended permeation enhancers should not be affected.

## BACKING MEMBRANE

Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, and accept printing. It is impermeable substance that protects the product during use on the skin e.g. metallic plastic laminate, plastic backing with absorbent pad and occlusive base plate (aluminium foil), adhesive foam pad (flexible polyurethane) with occlusive base plate (aluminium foil disc) etc.

## RELEASE LINER

During storage the patch is covered by a protective liner that is removed and discharged immediately before the application of the patch to skin it should comply with specific requirements regarding chemical inertness and permeation to the drug, penetration enhancer and water. It is composed of a base layer which may be non-occlusive (*e.g*. paper fabric) or occlusive (*e.g*. polyethylene, polyvinylchloride) and a release coating layer made up of silicon or teflon. Other materials used for TDDS release liner include polyester foil and metallized laminates

## DESIRABLE FEATURES FOR TRANSDERMAL PATCHES[9]

- Composition relatively invariant in use.
- System size reasonable.
- Defined site for application.
- Application technique highly reproducible.
- Delivery is (typically) zero order.
- Delivery is efficient

## INTRODUCTION OF CHEMICAL PENETRATION ENHANCERS19

The skin is very effective as a selective penetration barrier. Percutaneous absorption involves the passage of the drug molecule from the skin surface into the stratum corneum under the influence of a concentration gradient and its subsequent diffusion through the stratum corneum and underlying epidermis, through the dermis, and into the blood circulation. The skin behaves as a passive barrier to the penetrant molecule. The stratum corneum provides the greatest resistance to penetration, and it is the rate-limiting step in percutaneous absorption.Penetration enhancers are the substances that facilitate the absorption of penetrant through the skin by temporarily diminishing

the impermeability of the skin. Ideally, these materials should be pharmacologically inert, nontoxic, nonirritating, nonallergenic, compatible with the drug and excipients, odorless, tasteless, colorless, and inexpensive and have good solvent properties. The enhancer should not lead to the loss of body fluids, electrolytes, and other endogenous materials, and skin should immediately regain its barrier properties on its removal.

## IDEAL CHARACTERISTICS OF CHEMICAL PENETRATION ENHANCERS10

Penetration enhancers reversibly reduce the barrier resistance of the stratum corneum without damaging viable cells[11,12] Some of the more desirable properties for penetration enhancers acting within the skin have been given as:

- They should be non-toxic, non-irritating and non-allergenic
- They would ideally work rapidly; the activity and duration of effect should be both predictable and reproducible.
- They should have no pharmacological activity within the body.
- The penetration enhancers should workunidirectionally, i.e., they should allow therapeutic agents into the body whilst preventing the loss of endogenous materials from the body.
- When removed from the skin, barrier properties should return both rapidly and fully to normal.
- They should be cosmetically acceptable with an appropriate skin feel.

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## MECHANISM OF CHEMICAL PENETRATION ENHANCEMENT[10]

Penetration enhancers may act by one or more of three main mechanisms:
1. Disruption of the highly ordered structure of stratum corneum lipid.
2. Interaction with intercellular protein.
3. Improved partition of the drug, co enhancer or solvent into the stratum corneum.

The enhancer act by altering one of three pathways. The key to altering the polar pathway is to cause protein conformational change or solvent swelling. The fatty acid enhancers increased the fluidity of the lipid protein portion of the stratum corneum. Some enhancers act on both polar and nonpolar pathway by altering the multilaminate pathway for penetration. Enhancers can increase the drug diffusivity through skin proteins. The type of enhancer employed has a significant impact on the design and development of the product. A useful way to consider factors affecting drug permeation rate through the stratum corneum is via the simple equation given below for steady state flux. If we plot the cumulative mass of diffusant, *m*, passing per unit area through the membrane , at long the graph approaches linearity and its slope its yield the steady flux , *dm/dt*

$$dm/dt = D\ Co\ K\ /h \text{---------- (1)}$$

where *Co* is the constant concentration of drug in donor solution,

*K* is the partition coefficient of the solute between the membrane and the bathing solution,

*D* is the diffusion coefficient and *h* is thickness of membrane.

From the above equation, we deduce the ideal properties of a molecule that would penetrating stratum corneum well. These are:

- Low molecular mass, preferably less than 600Da, when D tends to be high.
- Adequate solubility in oil and water so that membrane concentration gradient may be high.
- High but balanced (optimal) K (if too large, may inhibit clearance by viable tissue)
- Low melting point, correlating with good solubility as predicted by ideal solubility
- theory.

## PREPARATION OF DIFFERENT TYPES OF TRANSDERMAL PATCHES:[13,14]

Several system designs have been used in development and fabrication of TDDSs.

- Matrix type
- Reservoir type
- Membrane matrix hybrid
- Micro reservoir type
- Drug in adhesive type

## MATRIX TYPE TRANSDERMAL PATCHES

Drug reservoir is prepared by dissolving the drug and polymer in a common solvent. The insoluble drug should be homogenously dispersed in hydrophilic or lipophillic polymer. The required quantity of plasticizer like

dibutylpthalate, triethylcitrate, polyethylene glycol or propylene glycol and permeation enhancer is then added and mixed properly. The medicated polymer formed is then molded into rings with defined surface area and controlled thickness over the mercury on horizontal surface followed by solvent evaporation at an elevated temperature. The film formed is then separated from the rings, which is then mounted onto an occlusive base plate in a compartment fabricated from a drug impermeable backing. Adhesive polymer is then spread along the circumference of the film. Commonly used polymers for matrix are cross linked polyethylene glycol, eudragits, ethyl cellulose, polyvinyl pyrrolidone and hydroxy propyl methyl cellulose.

The dispersion of drug particles in the polymer matrix can be accomplished by either homogenously mixing the finely ground drug particles with a liquid polymer or a highly viscous base polymer followed by cross linking of polymer chains or homogenously blending drug solids with a rubbery polymer at an elevated temperature.

## ADVANTAGES

- matrix patches include absence of dose dumping,
- direct exposure of polymeric matrix to the skin and
- no interference of adhesive.

Design of matrix type patch is shown in Figure 1.

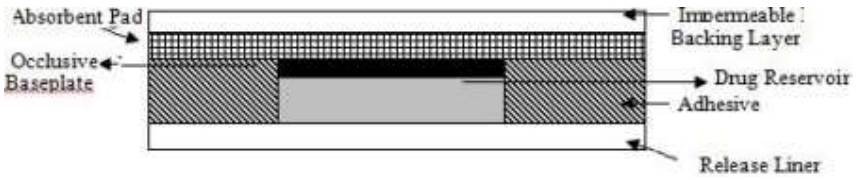


**Figure 1: Design of matrix type transdermal patch**

## RESERVOIR TYPE TRANSDERMAL PATCHES

The drug reservoir is made of a homogenous dispersion of drug particles suspended in an unleachable viscous liquid medium (e.g. silicon fluids) to form a paste like suspension or gel or a clear solution of drug in a releasable solvent (e. g. ethanol). The drug reservoir formed is sandwiched between a rate controlling membrane and backing laminate.

The rate controlling membrane can be nonporous so that the drug is released by diffusing directly through the material, or the material may contain fluid filled micropores in which case the drug may additionally diffuse through the fluid, thus filling the pores. In the case of nonporous membrane, the rate of passage of drug molecules depends on the solubility of the drug in the membrane and the thickness of membrane. Hence, the choice of membrane material is dependent on the type of drug being used. By varying the composition and thickness of the membrane, the dosage rate per unit area of the device can be controlled. Mostly EVA, ethyl cellulose, silicon rubber and polyurethanes are used to prepare rate controlling membranes. EVA is used most frequently to prepare rate controlling membrane in transdermal delivery systems because it allows the membrane permeability to be altered by adjusting vinyl acetate content of polymer. Polyurethane membranes are suitable especially for hydrophobic polar compounds having low permeability through hydrophobic polymers such as silicon rubber or EVA membrane.

Rate controlling membrane may be prepared by solvent evaporation method or compression method. In case of solvent evaporation method, polymer is dissolved in solvent with or without plasticizer. Then the solution is poured on the horizontal surface and left for evaporation of solvent in order to obtain a thin film. In case of compression method, polymer is compressed with required force at high temperature for specific period of time. Drugs that require relatively high doses or greater permeation enhancement, such as testosterone, use liquid reservoir systems. But the application of enhancers and adhesive technologies has allowed many drugs that were initially administered in liquid reservoirs to be used as matrix type systems e.g. estradiol, nicotine, nitroglycerine

## ADVANTAGE

This patch design can provide a true zero order release pattern to achieve a constant serum drug level.
Figure 2 illustrates the design of reservoir type of patch.

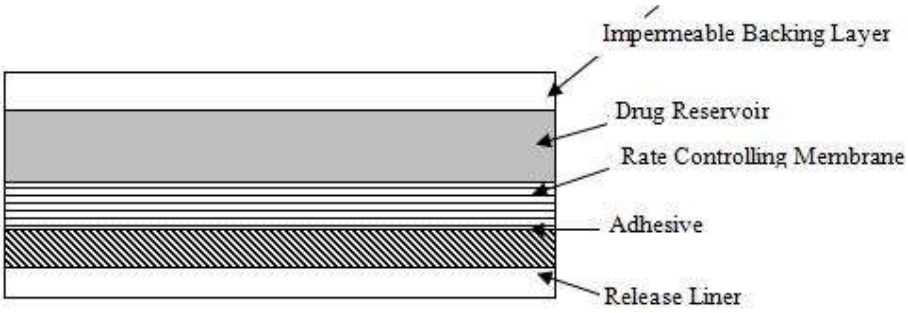


**Figure 2: Design of reservoir type transdermal patch**

## MEMBRANE MATRIX HYBRID TYPE PATCHES

This is the modification of reservoir type transdermal patch. The liquid formulation of the drug reservoir is replaced with a solid polymer matrix (e.g. polyisobutylene) which is sandwiched between rate controlling membrane and backing laminate.

## MICRO RESERVOIR TYPE TRANSDERMAL PATCHES

The drug reservoir is formed by suspending the drug solids in an aqueous solution of water miscible drug solubilizer e.g. polyethylene glycol. The drug suspension is homogenously dispersed by a high shear mechanical force in lipophillic polymer, forming thousands of unleachable microscopic drug reservoirs (micro reservoirs). The dispersion is quickly stabilized by immediately cross linking the polymer chains in-situ which produces a medicated polymer disc of a specific area and fixed thickness. Occlusive base plate mounted between the medicated disc and adhesive form backing prevents the loss of drug through the backing membrane. Micro reservoir type transdermal system is shown in Figure

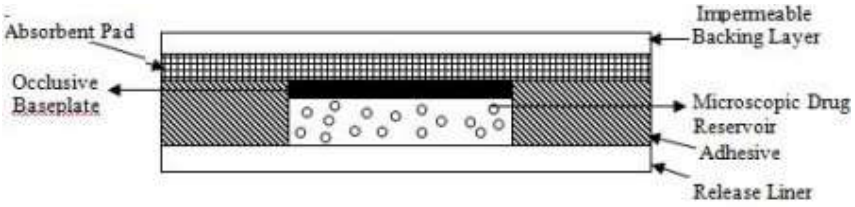


**Figure 3: Design of micro reservoir type transdermal patch**

## DRUG IN ADHESIVE TYPE TRANSDERMAL PATCHES

The drug and other selected excipients, if any, are directly incorporated into the organic solvent based pressure sensitive adhesive solution, mixed, cast as a thin film and dried to evaporate the solvents, leaving a dried adhesive matrix film containing the drug and excipients. This drug in adhesive matrix is sandwiched between release liner and backing layer. Drug -in -adhesive patch may be single layer or multi layer. The multi layer system is different from single layer in that it adds another layer of drug-in-adhesive, usually separated by a membrane.
Some examples of suitable pressure sensitive adhesives are polysiloxanes, polyacrylates and polyisobutylene. These pressure sensitive adhesives are hydrophobic in nature and are prepared as solutions of polymer dissolved in organic solvents. Hence, this type of system is preferred for hydrophobic drugs as it is to be incorporated into organic solvent based hydrophobic adhesive. Characteristics of drug in adhesive patch may account for improved patient compliance due to ease of remembering once weekly patch application, improved cosmetic acceptance and better adhesion. Design of this system is shown in Figure 4.

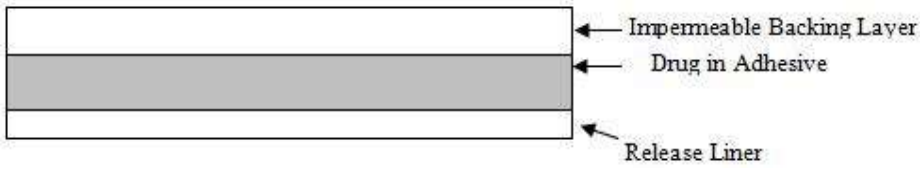


**Figure 4: Design of drug in adhesive type transdermal patch**

## EVALUATION

The evaluation of TDDS involves

- Physicochemical evaluation
- *In vitro* evaluation
- *In vivo* evaluation

## PHYSICOCHEMICAL EVALUATION

**Thickness:** The thickness of transdermal film is determined by traveling microscope, dial gauge, screw gauge or micrometer at different points of the film.

**Uniformity of weight:** Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.

**Drug content determination:** An accurately weighed portion of film (about 100 mg) is dissolved in 100 mL of suitable solvent in which drug is soluble and then the solution is shaken continuously for 24 h in shaker incubator. Then the whole solution is sonicated. After sonication and subsequent filtration, drug in solution is estimated spectrophotometrically by appropriate dilution.

**Content uniformity test:** 10 patches are selected and content is determined for individual patches. If 9 out of 10 patches have content between 85% to 115% of the specified value and one has content not less than 75% to 125% of the specified value, then transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75% to 125%, then additional 20 patches are tested for drug content. If these 20 patches have range from 85% to 115%, then the transdermal patches pass the test.

**Moisture content:** The prepared films are weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 h. The films are weighed again after a specified interval until they show a constant weight. The percent moisture content is calculated using following formula[24].

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

**Moisture Uptake:** Weighed films are kept in a desiccator at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using saturated solution of Potassium chloride in a desiccator until a constant weight is achieved. % moisture uptake is calculated as given below[24].

$$\% \text{ moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

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

$$\% \text{ constriction} = \frac{I_1 - I_2}{I_1} \times 100 \qquad (1)$$

$I_2$ = Final length of each strip

$I_1$ = Initial length of each strip

**Folding Endurance:** Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. Folding endurance is determined by repeatedly folding the film at the same place until it break. The number of times the films could be folded at the same place without breaking is folding endurance value.

**Tensile Strength:** To determine tensile strength, polymeric films are sandwiched separately by corked linear iron plates. One end of the films is kept fixed with the help of an iron screen and other end is connected to a freely movable thread over a pulley. The weights are added gradually to the pan attached with the hanging end of the thread. A pointer on the thread is used to measure the elongation of the film. The weight just sufficient to break the film is noted. The tensile strength can be calculated using the following equation.

Tensile strength= F/a.b (1+L/l) (2)

F is the force required to break; a is width of film; b is thickness of film; L is length of film; l is elongation of film at break point

In another study, Tensile strength of the film was determined with the help of texture analyzer[70]. The force and elongation were measured when the films broke.

Water vapor transmission studies (WVT):

For the determination of WVT, Rao *et al*., (1997) weighed one gram of calcium chloride and placed it in previously dried empty vials having equal diameter. The polymer films were pasted over the brim with the help of adhesive like silicon adhesive grease and the adhesive was allowed to set for 5 minutes. Then, the vials were accurately weighed and placed in humidity chamber maintained at 68 % RH. The vials were again weighed at the end of every 1st day, 2nd day, 3rd day up to 7 consecutive days and an increase in weight was considered as a quantitative measure of moisture transmitted through the patch.

In other reported method, desiccators were used to place vials, in which 200 mL of saturated sodium bromide and saturated potassium chloride solution were placed. The desiccators were tightly closed and humidity inside the desiccator was measured by using hygrometer. The weighed vials were then placed in desiccator and procedure was repeated.

WVT = W/ ST (3)

W is the increase in weight in 24 h; S is area of film exposed ($cm^2$); T is exposure time

**Microscopic studies:** Distribution of drug and polymer in the film can be studied using scanning electron microscope. For this study, the sections of each sample are cut and then mounted onto stubs using double sided adhesive tape. The sections are then coated with gold palladium alloy using fine coat ion sputter to render them electrically conductive. Then the sections are examined under scanning electron microscope

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