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A REVIEW ARTICLE ON TRANSDRMAL DRUG DELIVERY SYSTEM

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Abstract:
A transdermal patch is an adhesive that has been medicated and applied to the skin to transfer a predetermined dosage of medication through the skin and into the bloodstream. Several non-invasive administrations have recently emerged as alternatives to conventional needle injections. TDDS has potential applications not only in the pharmaceutical industry but also in the skincare industry, which encompasses cosmetics. With an average adult's surface area of 2 m^2, the skin receives about 1/3 of the blood that flows through the body. Over the past few decades, the development of controlled medication delivery has gained importance in the pharmaceutical industry. Per square centimetre, there are typically 200–250 sweat ducts and 10–70 hair follicles on the surface of human body.

KEYWORD: TDDS, the pharmaceutical industry used, skin care.

Introduction:

Scopolamine was the medication used in the first transdermal drug delivery (TDD) system, transdermal-scope, which was created in 1980 to alleviate motion sickness. Transdermal drug delivery systems, or "patches," are self-contained, discrete dosage forms that, when placed on undamaged skin, transfer medications to the systemic circulation at a controlled rate through the skin[8,9.] Transdermal drug delivery systems aim to administer medications at a present rate through the skin to the systemic circulation with the least amount of fluctuation between and within patients. It lessens the strain that eating orally frequently puts on the liver and digestive system. [1,3]

The common ingredients which are used for the preparation of TDDS are as follows:

Drug: The drug is in direct contact with release liner Ex: nicotine, methotrexate, and estrogen.
Liner: protects the patch during storage .ex: polyester film.
Adhesive: serves to adhere the patch to the skin for systemic delivery of the drug.
Ex: Acrylates, polyisobutylene, silicones.
Permeation enhancers: control the release of the drug. Ex: terpenes, pyrrolidones solvents like alcohol, ethanol, methanol, surfactants like sodium lauryl sulphate, pluronic F123, pluronic F68.
Backing layer: Protect the patch from the outer environment. Ex: Cellulose derivatives, polyvinyl alcohol, Polypropylene Silicon rubber.

Transdermal drug delivery system (TDDS) benefits include:

It is possible to self-medicate.
avoiding the drug's first-pass metabolism.
medicines with lower plasma concentration levels and fewer negative effects.
lowering medication variations in the plasma levels and using pharmacological candidates with low therapeutic indices and short half-lives.
Drug distribution can be easily stopped in the event of toxicity.
decrease in dosage frequency and improvement in patient adherence.
Transdermal drugs provide a continuous infusion of treatment over a long duration.
Additionally, since irregular dosing is frequently associated with adverse effects or therapeutic failure, it is possible to avoid them.

The transdermal medication delivery system has certain drawbacks

1. Potential for an allergic response.
2. A medication with a high molecular level cannot reach a therapeutic level.
3. It is given as an ionic medication.
4. There is a noticeable lag time.
5. Ionic medicines cannot be administered by transdermal drug delivery systems.
6. It is unable to produce elevated blood drug levels.
7. It cannot grow for medications with big molecular weights.
8. It is unable to provide medication in a pulsating manner.
9. If the medicine or formulation irritates the skin, it cannot develop.
10. Local discomfort at the application location is a possibility.
11. May cause allergic reactions.[10,11,12]

Anatomy and physiology of skin: Human skin consists of three distinct which are discussed follow as: -

1. The stratified, vascular, cellular epidermis,
2. Underlying dermis of connective tissues and Hypodermis.[2]

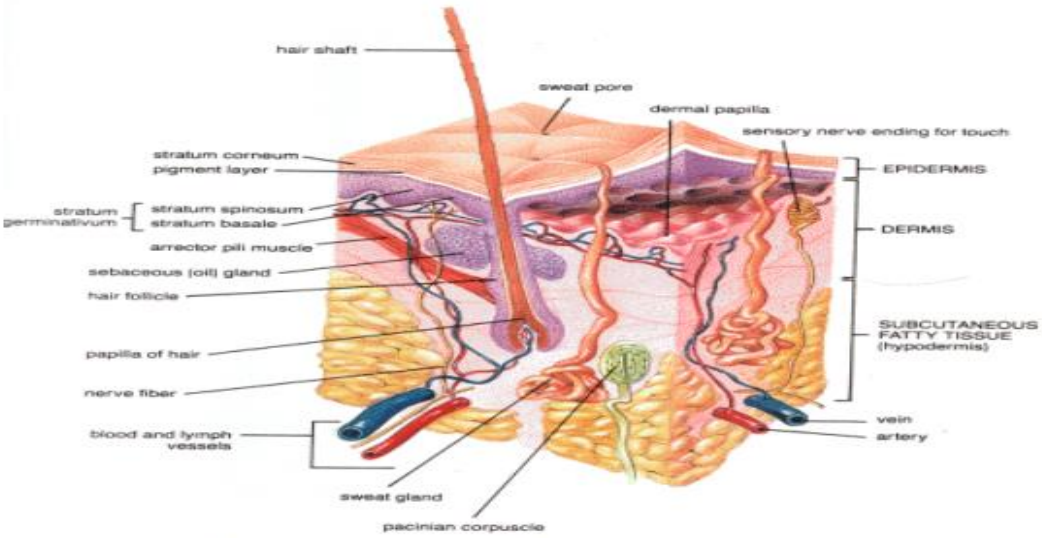


Figure 1: Structure of skin

1)Epidermis: - The keratinizing, squamous, stratified epidermal epithelium. The thickness, size, and quantity of cells that make up the epidermis's complex layer vary, ranging from 0.8 mm on the palms and soles to 0.06 mm on the eyelids. Melanocytes make up 8% of epidermal cells, while keratinocytes, or cells rated in five layers on the chest, make up about 90% of epidermal cells. They produce yellow or dark-colored melanin, which contributes to skin darkening and absorbs harmful UV rays. From red bone marrow, a Langerhans cell proliferates and migrates to the epidermis, where it makes up a small fraction of epidermis cells. The smallest group of epidermal cells is called Markel cells. As illustrated in Fig.2 viable epidermis is further divided into four different layers.
Stratum lucidum
Stratum granulosum
Stratum spinosum
Stratum basale[6,7]

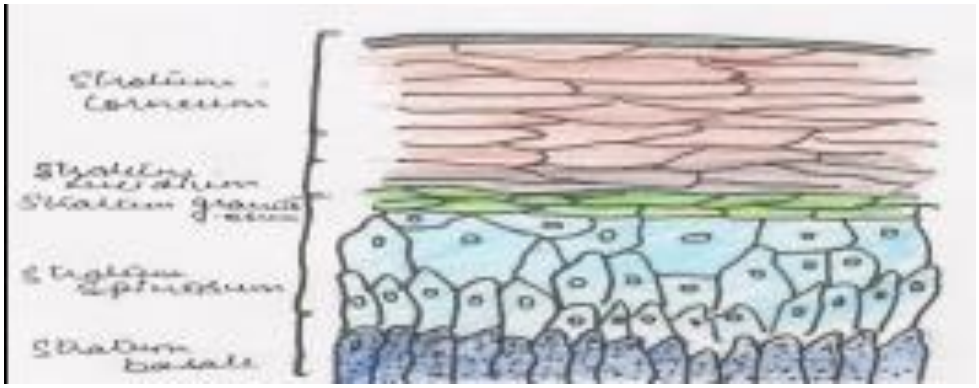
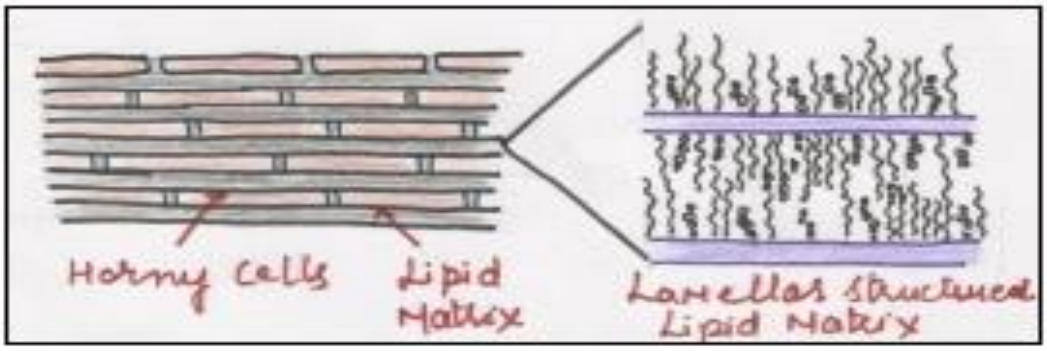


FIG 2.**:** SCHEMATIC REPRESENTATION OF ANATOMY OF EPIDERMIS

Stratum corneum:
This is the skin's outermost layer, sometimes known as the horny layer. The barrier that limits the flow of chemicals both inward and outward is known as the rate-limiting barrier. The horny layer's ability to act as a barrier is heavily dependent on its components: On a dry weight basis, there are 75–80% proteins, 5–15% lipids, and 5–10% ondansetron material. When completely hydrated, the stratum corneum swells to several times its dry thickness of about 10 mm. Although flexible, it is not very porous. With protein bricks and lipid mortar, the architecture of the horny layer (figure 3) can be represented as a wall-like structure. It is made up of horny skin cells called corneocytes that are linked together by desmosomes, which are membrane-bound appendages that are rich in proteins. Being immersed in a lipid matrix, the corneocytes play a significant role in determining the permeability of substances across the skin.[18]



1. 3: SCHEMATIC REPRESENTATION OF MICROSTRUCTURE OF STRATUM CORNEUM.

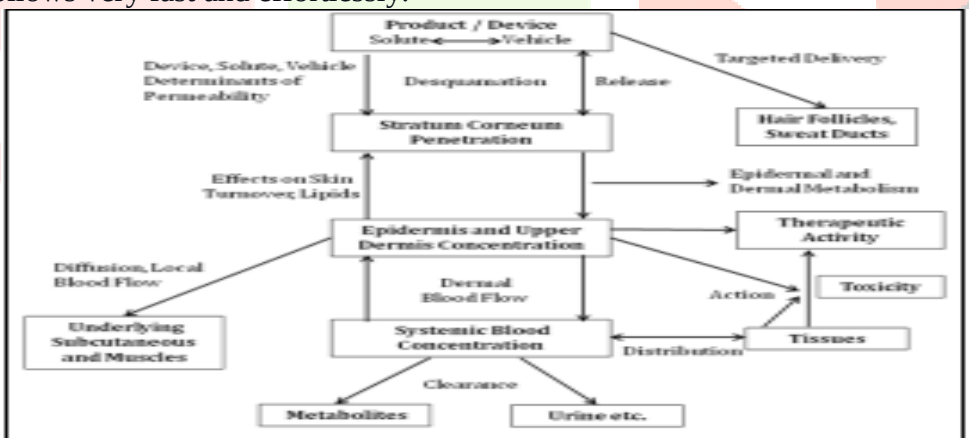
Viable epidermis: This varies in thickness from 0.06 mm on the eyelids to 0.8 mm on the palms and is located under the stratum corneum. It is made up of several layers that go inward, including the stratum basale, stratum lucidum, stratum granulosum, and stratum spinosum. The epidermis at the basal layer is continuously renewed by cell mitosis, which makes up for the loss of dead horny cells from the skin's surface. The basal layer produces cells that migrate outward, changing in morphology and histochemistry as they go through keratinization to form the stratum corneum's outermost layer.

1. 4: SCHEMATIC REPRESENTATION OF DIFFERENT LAYERS OF EPIDERMIS

Dermis: The dermis is a 3 to 5-mm thick layer of skin that lies just below the epidermis. It is made up of a matrix of connective tissues that contains blood and lymph vessels, nourishes the skin with nutrients and oxygen, and removes waste products and pollutants. Capillaries can access nerves. The control of body temperature relies heavily on the cutaneous blood supply. Additionally, it gets to within 0.2 mm of the skin's surface and offers circumstances that allow most molecules to sink through the skin barrier. Thus, the blood supply maintains a relatively low dermal permeate concentration, and the consequent concentration differential across Transdermal permeation has its primary source of energy in the epidermis. The dermal barrier may be important when delivering highly lipophilic compounds because this layer is sometimes thought of as essentially gelled water in terms of transdermal drug administration and thus presents a minor barrier to the transport of most polar medicines.

1)Hypodermis: The dermis and epidermis are supported by the hypodermis or subcutaneous fat tissue. It functions as a place to store fat. This layer offers mechanical protection, nutrient support, and assistance with temperature regulation. Principal blood arteries, nerves, and possibly pressure-sensing organs are carried there to the skin. To be effective for transdermal medicine delivery, a substance must pass through all three layers and enter the bloodstream.

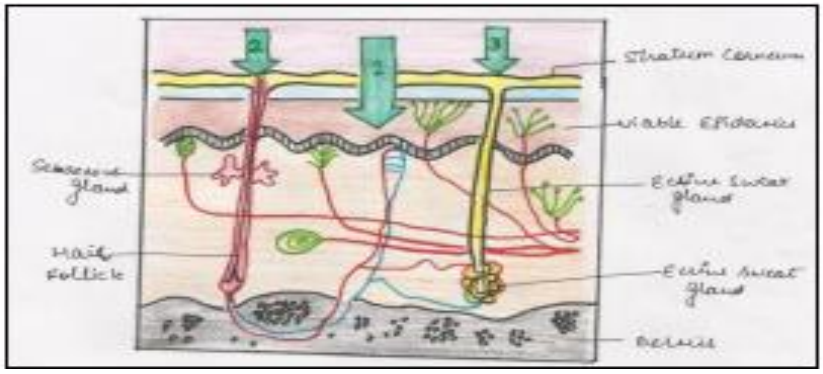
1. **Percutaneous absorptions: -** A medicine applied topically must permeate the stratum corneum before it may operate locally or systemically. The definition of percutaneous absorption is the passage of chemicals through the skin's layers and into the systemic circulation.11 Because the drug must be absorbed sufficiently to achieve and maintain constant, systemic, therapeutic levels throughout use, percutaneous drug absorption is particularly crucial in transdermal drug delivery systems. Drug molecules often penetrate through the stratum corneal barrier, and deeper dermal layers, and systemic uptake follows very fast and effortlessly.



5: SCHEMATIC REPRESENTATION OF PERCUTANEOUS PERMEATION.

The dissolution within and release from the formulation are two steps in the multistep process (figure 5) that result in the release of a therapeutic agent from a formulation applied to the skin surface and its transportation to the systemic circulation.
insertion into the stratum corneum (SC), the skin's topmost layer
diffusion primarily by a lipidic intercellular route through the SC.
the SC is partitioned into the aqueous viable epidermis, the viable epidermis is diffused into the upper dermis, the upper dermis is uptaken into the papillary dermis (capillary system), and the microcirculation is then affected.

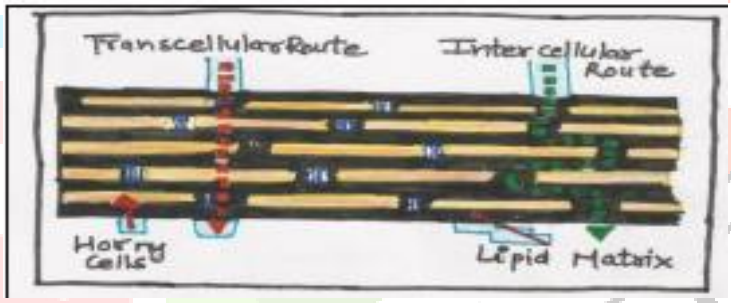
3) Routes of drug penetration through the skin: In the process of percutaneous permeation, a drug molecule may pass through the epidermis itself or may diffuse through shunts, particularly those offered by the relatively widely distributed hair follicles and endocrine glands, as shown in figure 6. In the initial transient diffusion stage, drug molecules may penetrate the skin along the hair follicles or sweat ducts and then be absorbed through the follicular epithelium and the sebaceous glands. When a steady state has been reached, diffusion through the intact stratum corneum becomes the primary pathway for transdermal permeation.



1. 6: POSSIBLE MACRO ROUTES FOR DRUG PENETRATION 1) INTACT HORNY LAYER, 2) HAIR FOLLICLES AND 3) ENDOCRINE SWEAT GLANDS.

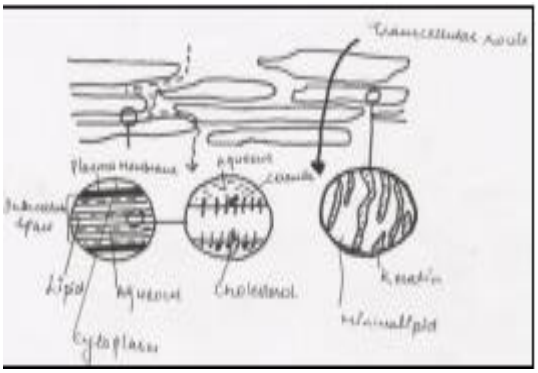
For any molecules applied to the skin, two main routes of skin permeation can be defined: Trans epidermal route
Trans follicular route

1. **Trans epidermal route**: In transepidermal transport, molecules cross the intact horny layer. Two potential micro-routes of entry exist, the transcellular (or intracellular) and the intercellular pathway.



7: SCHEMATIC REPRESENTATION OF TRANSEPIDERMAL ROUTE

Both polar and non-polar substances diffuse via transcellular and intercellular routes by different mechanisms. The polar molecules mainly diffuse through the polar pathway consisting of “bound water” within the hydrated stratum corneum, whereas the non-polar molecules dissolve and diffuse through the non-aqueous lipid matrix of the stratum corneum.
Thus the principal pathway taken by a penetrate is decided mainly by the partition coefficient (log K). Hydrophilic drugs partition preferentially into the intracellular domains, whereas lipophilic permanent (octanol/water log K > 2) traverse the stratum corneum via the intercellular route. Most molecules pass the stratum corneum by both routes.



8: POSSIBLE MICRO ROUTES FOR DRUG PENETRATION ACROSS HUMAN SKIN INTERCELLULAR OR TRANSCELLULAR.

2. Transfollicular route (Shunt pathway): This route comprises transport via the sweat glands and the hair follicles with their associated sebaceous glands. Although these routes offer high permeability, they are considered to be of minor importance because of their relatively small area, approximately 0.1% of the total skin. This route seems to be most important for ions and large polar molecules, which hardly permeate through the stratum corneum.[17]

4) Barrier functions of the skin: The most crucial component in maintaining the barrier's efficacy is the top layer of skin. The skin's ability to retain water is preserved because the individual cells are closely packed and overlap one another in this area14. In contrast to the other skin components, the stratum corneum primarily consists of keratinized dead skin cells and has a lower water content.15 From the skin's deepest layers to its surface, cells release lipids. These lipid molecules combine to create a strong connective network that serves as the mortar between a wall's bricks.

5) Basic Principal of Transdermal permeation: On passive diffusion, transdermal permeation is based1. With only a few hundredths of a millimeter of tissue separating its surface from the underlying capillary network, the skin is the human organ that is most intensive and easily accessible.7 Several steps must be completed before a therapeutic agent is released from a formulation applied to the skin surface and transported into the systemic circulation. These steps are as follows:

1. Diffusion of drug from drug to the rate controlling membrane.
2. Dissolution within and release from the formulation.
3. Sorption by stratum corneum and penetration through viable epidermis.
4. Uptake of the drug by capillary network in the dermal papillary layer.
5. Effect on the target organ.
6. Partitioning into the skin’s outermost layer, the stratum corneum.
7. Diffusion through the stratum corneum, principal via a lipidic intercellular pathway.

Table 1: Regional variation in water permeability of stratum corneum

Sr. No.	Skin region	Thickness (µm)	Permeation rate (mg/ cm²/hr)	Diffusivity (cm²/sec × 10¹⁰)
1	Abdomen	15.0	0.34	6.0
2	Volar forearm	16.0	0.31	5.9
3	Back	10.5	0.29	3.5
4	Forehead	13.0	0.85	12.9
5	Scrotum	5.0	1.70	7.4
6	Back of hand	49.0	0.56	32.3
7	Palm	400.0	1.14	535.0
8	Plantar	600.0	3.90	930.0

B-Intracellular versus transcellular diffusion

Figure 3: The microstructure of stratum corneum
Intracellular regions in the stratum corneum are filled with lipid-rich amorphous material. In dry stratum corneum, intracellular volume may be 5% to 1% in full hC. Permeation pathways 7-9 Percutaneous absorption involves passive diffusion of the substances through the skin. A molecule may use two diffusional routes to penetrate normal intact skin, the appendageal route and the epidermal route.

1. **Appendageal route:** Transport via sweat glands and hair follicles with related sebaceous glands makes up the appendageal route. These paths are referred to as "shunt" routes because they avoid penetrating the stratum corneum. Due to its tiny size—roughly 0.1% of the overall skin area—this pathway is regarded as being of secondary relevance. Stratum Corneum Hydrated

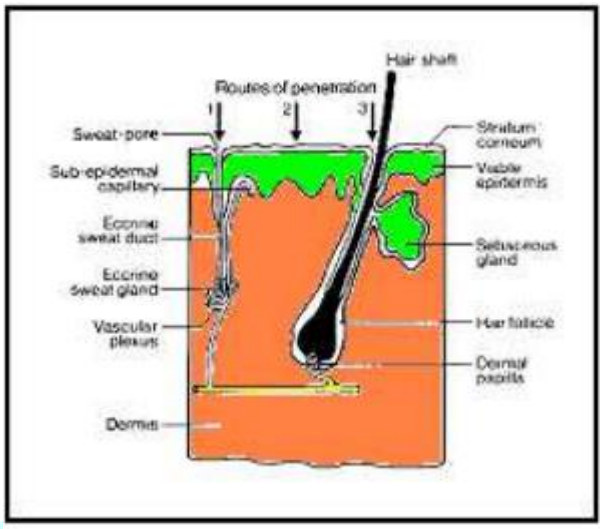


Figure 4: Routes for drug permeation

2. Epidermal route: The transcellular (intracellular) and intercellular pathways are two potential micro-routes of entry for medicines that mostly traverse the horney layer.

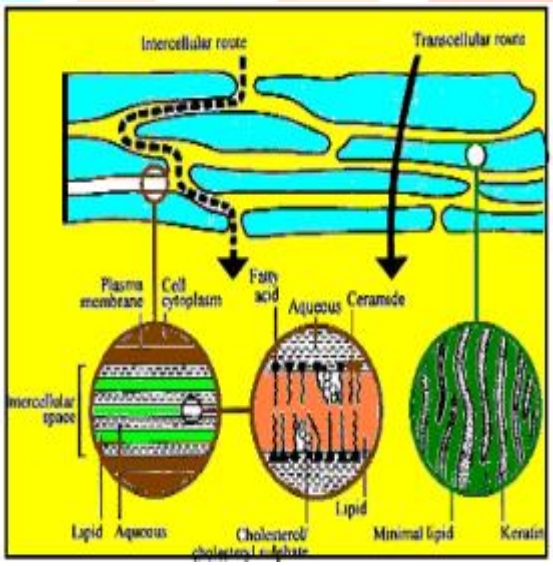


Figure 5: Epidermal routes for drug permeation.

i)Transcellular: The transcellular route refers to the movement of chemicals over the cellular membrane of the epithelium. Small molecule passive transport, ion and polar compound active transport, and macro-molecule endocytosis and transcytosis are a few of them.

1. **Paracellular:** The term "paracellular pathway" refers to the movement of chemicals inside or outside of cells. The cells are connected by tight junctions or other comparable conditions. The partition coefficient (log k) mostly determines the major path that a permanent take. While lipophilic permanent goes through the stratum corneum via the intercellular pathway, hydrophilic medicines preferentially partition into the intracellular domains. The majority of permanent enter the stratum corneum via both methods. The convoluted intercellular pathway is thought by many to be the main conduit and a significant obstacle to the penetration of most medicines.

Factors that influence transdermal drug delivery: [-14,15]
Three elements drug, skin, and vehicles can be combined to create an efficient transdermal drug delivery system. As a result, the influencing elements can be further classified into two classes: biological factors and Physicochemical factors.

Biological Factors Include:

1. Skin condition.
2. Skin age.
3. Blood flow.
4. Regional skin sites.
5. Skin metabolism.
6. Species differences.

Physiological Factors Include:

1. Skin hydration.
2. Temperature and pH
3. Diffusion coefficient.
4. Drug concentration.
5. Partition coefficient.
6. Molecular size and shape.

A**. Biological factors**:

1.Skin condition: Acids and alkali, many solvents like chloroform, and methanol damage the skin cells and promote penetration. The diseased state of the patient alters the skin conditions. The intact skin is a better barrier but the above-mentioned conditions affect penetration.

2.Skin age: The young skin is more permeable than older. Children are more sensitive to skin absorption of toxins. Thus, skin age is one of the factors affecting the penetration of drugs in TDDS.

3.Blood supply: Changes in peripheral circulation can affect transdermal absorption.

4.Regional skin site: Thickness of skin, nature of stratum corneum and density of appendages vary from site to site. These factors affect significantly penetration.

5.Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens, and some drugs. So skin metabolism determines the efficacy of drugs permeated through the skin.

6.Species differences: The skin thickness, density of appendages, and keratinization of skin vary from species to species, so affects the penetration.

B. Physicochemical factors:

1. **Skin hydration:** In contact with water the permeability of the skin increases significantly. Hydration is the most important factor in increasing the permeation of skin. So use of humectant is done in transdermal delivery.
2. **Temperature and pH:** The permeation of the drug increases tenfold with temperature variation. The diffusion coefficient decreases as the temperature falls. Weak acids and weak bases dissociate depending on the pH and pKa or pKb values. The proportion of unionized drugs determines the drug concentration in the skin. Thus, temperature and pH are important factors affecting drug penetration.
3. **Diffusion coefficient:** Penetration of a drug depends on the diffusion coefficient of the drug. At a constant temperature, the diffusion coefficient of the drug depends on the properties of the drug, the diffusion medium, and the interaction between them.
4. **Drug concentration:** The flux is proportional to the concentration gradient across the barrier and the concentration gradient will be higher if the concentration of the drug is higher across the barrier.
5. **Partition coefficient:** The optimal partition coefficient (K) is required for good action. Drugs with high K are not ready to leave the lipid portion of the skin. Also, drugs with low K will not be permeated.

6. **Molecular size and shape**: Drug absorption is inversely related to molecular weight; small molecules penetrate faster than large ones.

Ideal molecular properties for transdermal drug delivery:

We can draw some conclusions about the optimum molecular characteristics for medication penetration from the aforementioned factors. They are listed below.
A sufficient solubility in lipid and water is required for the drug's (1 mg/ml) greater penetration.
The partition coefficient must be at its ideal level for effective therapeutic activity.
The medication should have a low melting point (2000c).
The saturated solution's pH should range from 5 to 9**.**

Design of transdermal delivery system: - A drug that has been dissolved or distributed in an inert polymer matrix, which serves as support and a platform for drug release, is one of the fundamental components of any transdermal delivery system.
The patch system's two fundamental designs, which determine the nature of drug release and patch behavior, are as follows:

Matrix or Monolithic: The medicine is bound to the inert polymer matrix, which also regulates the drug's release from the device.

Reservoir or Membrane: The release of drugs is not regulated by the polymer matrix. The rate-limiting barrier for drug release from the device is now provided by a rate-controlling membrane that is present between the drug matrix and the sticky layer. systems for creating transdermal medication delivery technologies.

Parameter	Properties
Dose	Less than 20mg/day
Halflife	< 10 hrs
Molecular weight	<400 Dalton
Melting point	<200°C
Partition coefficient	1 to 4
Aqueous Solubility	>1mg/mL
pH of the aqueous saturated solution	5-9
Skin Permeability Coefficient	$>0.5\times10^{-3}$cm/h
Skin Reaction	Non irritating and non-sensitizing
Oral Bioavailability	Low

TABLE 1: IDEAL PROPERTIES OF DRUG CANDIDATE FOR TRANSDERMAL DRUG DELIVERY.

Polymer matrix:
Polymers are the foundation of the transdermal medication delivery technique. Polymeric laminates, a term for systems for transdermal distribution comprised of numerous polymeric layers, are used. A drug reservoir or drug-polymer matrix is sandwiched between two polymeric layers: an inner polymeric layer that functions as an adhesive or rate-controlled membrane and an exterior polymeric layer that acts as an impermeable backing layer to prevent drug loss via the backing surface. The ideal characteristics of a polymer for a transdermal system are:
l The polymer's molecular weight and chemical activity should be chosen such that the particular medicine may diffuse and be released through it effectively.
l The polymer needs to be reliable.
l The polymer ought to be safe for use.
l It should be simple to make the polymer.
l The polymer must be reasonably priced.
l Both the polymer and the result of its degradation must not be poisonous or hostile to the host.
l It contains significant levels of the active ingredient.

Table 2 lists many commonly used polymers for TDDS.

Natural Polymers	Synthetic Elastomers	Synthetic Polymers
Cellulose derivatives	Polybutadiene	Polyvinylalcohol
Arabino Galactan	Hydrinrubber	Polyethylene
Zein	Polysiloxane	Polyviny Chloride
Gelatin	Acrylonitrile	Polyacrylates
Proteins	Neoprene	Polyamide
Shellac	Chloroprene	Acetal copolymer
Strarch	Silicon rubber	Polysyrene

TABLE 2: USEFUL POLYMERS FOR TRANSDERMAL DEVICES

Penetration Enhancers: These are compounds that promote skin permeability by altering the skin as a barrier to the flux of a desired penetrate.

Ideal properties of penetration enhancers:

- Controlled and reversible enhancing action
- Chemical and physical compatibility with drug and other pharmaceutical excipients
- Should not cause loss of body fluids, electrolytes, or other endogenous materials
- Non-toxic, non-allergic, non-irritating
- Pharmacological inertness
- Ability to act specifically for a predictable duration
- Odourless, colorless, economical, and cosmetically acceptable.

Some commonly used absorption enhancers for TDD are shown.

Class	Examples	Mechanism	Transport Pathway
Surfactants	Na-lauryl sulfate	Transcellular	Phospholipid acyl chain perturbation
	Polyoxyethylene-9-laurylether, Bile salts:		
	Na-deoxycholate	Paracellular	Reduction mucus viscosity, Peptidase inhibition
	Na-glycocholate		
	Na-taurocholate		
Fatty acids	Oleic acid,	Transcellular	Phospholipid acyl chain perturbation
	Short fatty acids	Paracellular	
Cyclodextrins	α-, β- and γ cyclodextrins, Methylated β cyclodextrins	Transcelular	Inclusion of membrane compounds
		Paracellular	
Chelating agents	EDTA,	Transcellular	Complexation of Ca^{2+} opening of tight junctions
	Polyacrylates	Paracellular	
Positively charged polymer	Chitosan salts, Trimethyl chitosan	Paracellular	Ionic interactions with negatively charged groups of glycocalix

Table3.TYPESOFABSORPTIONENHANCERS.

Other excipients: To produce the drug reservoir, a variety of solvents including chloroform, methanol, acetone, isopropanol, and dichloromethane are utilized. Additionally, plasticizers such as dibutyl phthalate and polypropylene glycol are added to the transdermal patch to give it plasticity.

Pressure-sensitive adhesive: A substance called a Pressure Sensitive Adhesive (PSA) aids in preserving close contact between a transdermal system and the skin's surface. It should be forcefully and permanently tacky, adhere with no more than finger pressure, and exert a strong holding force. Furthermore, it must be removed from the flat surface without leaving a trace. 7 Examples include silicone-based glue, polyacrylates, polyacrylates, and polyisobutylene. Numerous elements, such as the patch design and drug formulation, influence the choice of adhesive. PSA shouldn't affect drug release and should be compatible with biology and physics. The PSA can be placed on the device's front or back, stretching outward in either direction

2 Backing laminates: While designing a backing layer the consideration of chemical resistance7 and excipients may be compatible because of the prolonged contact between the backing layer and the excipients, drug, or penetration enhancer through the layer. They should have a low moisture vapour transmission rate. They must have optimal elasticity, flexibility, and tensile strength. Eg: an aluminium vapour-coated layer, a plastic film, and a heat-real layer. Release linear: During storage release linear prevents the loss of drug that has migrated into the adhesive layer and contamination. However, as the linear is in intimate contact with the delivery system, it should comply with specific requirements regarding chemical inertness and permeation to the drug, penetration enhancer, and water.

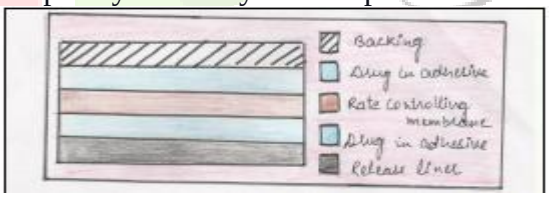
Major transdermal systems:

A). **Drug in adhesive system:**

l **Single-layer drug in adhesive**: The adhesive layer of this system contains the drug. In this type of patch, the adhesive layer not only serves to adhere the entire various layers together, along with a system to the skin but is also responsible for releasing the drug. The rate of release of drugs from this type of system is dependent on the diffusion across the skin. The adhesive layer is surrounded by a temporary linear and a backing layer.

Shown in Fig.: SINGLE LAYER ADHESIVE TRANSDERMAL DELIVERY SYSTEM

2. **Multi-layer drug in adhesion**: The multi-layer drug-in adhesive patch is similar to the single-layer system in that both adhesive layers are also responsible for the releasing of the drug 8 shown in Fig. 11. One of the layer is for the immediate release of the drug and other layer is for control release of drug from the reservoir. The multi-layer patch also has a temporary linear layer and a permanent backing.[12]



11: MULTILAYERED DRUG IN ADHESIVE TRANSDERMAL SYSTEM.

Reservoir: Unlike the single layer and multilayer drug in adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing layer, in Fig. 12 In this type of system the rate of release is zero order.[13]

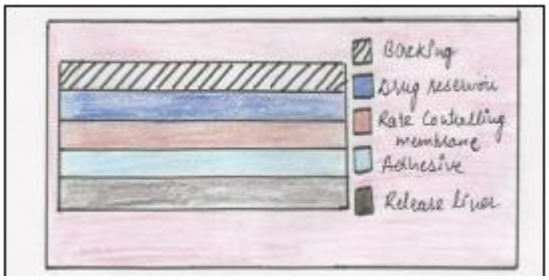
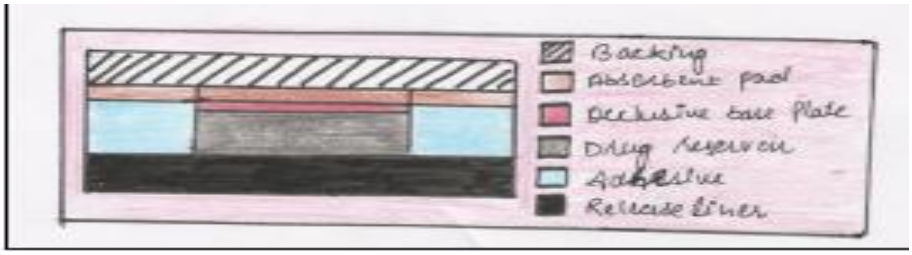


FIG.12: SCHEMATIC REPRESENTATION OF RESERVOIR TRANSDERMAL DELIVERY SYSTEM.

Matrix: The Matrix system design as shown in Fig. 13 has a drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlying it. These types of patches are also known as monolithic devices.[13]



13: SCHEMATIC REPRESENTATION OF MATRIX TRANSDERMAL DELIVERY SYSTEM13.4

Vapour Patch: In this type of patch the adhesive layer not only serves to adhere the various layers together but also to release vapour. The vapour patches are new on the market and they release essential oils for up to 6 hours. The vapour patches release essential oils and are used in cases of decongestion mainly.8 Other vapour patches on the market are controlled vapour patches that improve the quality of sleep 20 Vapour patches that reduce the quantity of cigarettes that one smokes in a mouth are also available on the market.[19]

Various methods for the preparation of transdermal drug delivery system:

Mercury substrate method: In this method, the drug is dissolved in a polymer solution along with a plasticizer. The above solution is to be stirred for 10-15 min to produce a homogeneous dispersion and poured into a leveled mercury surface. Then the solution is covered with an inverted funnel to control solvent evaporation.[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 the preparation of the same, chloroform is the choice of solvent because most drugs as well as adhesives 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 are blanked off with tightly fitting cork blocks.[9,16]

Limitation:

1. It cannot administer a drug that requires high blood levels.
2. Drug or drug formulation may cause skin irritation and sensitization.
3. The barrier function of the skin changes from one site to another on the same person, from person to person, and with age.
4. Not practical, when the drug is extensively metabolized in the skin and when molecular size is great enough to prevent the molecules from diffusing through the skin.
5. May cause allergic reactions.
6. Long-time adherence is difficult. [4,5]

Conclusion:

TDDS is used for drug therapy for less absorption, more uniform plasma levels, improved bioavailability, decreased side effects, efficacy, and quality of the product. A patch has some simple components, which perform a vital role in the release of drugs through the skin. Future prospective of TDDS would be focused on controlled therapeutic use.

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