

A Concise Summary of Transdermal Patches

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Abstract: *Transdermal patches offer a method of drug delivery that does not require penetration of the skin. It is a patch with adhesive properties that releases a controlled amount of medication into the bloodstream via the skin. Transdermal drug delivery offers numerous benefits when compared to alternative methods of administration. It is less invasive, more patient-friendly, and can avoid the harsh acidic condition of the stomach that drugs are exposed to when taken orally. Transdermal patches have been a focus of interest and have been utilized for many years to administer medication like nicotine, fentanyl, nitroglycerin, and clonidine for the treatment of different illnesses or ailments. For millennia, human societies have used various substances on the skin for cosmetic and medicinal purposes. Nevertheless, it wasn't until the 20th century that the skin started being utilized as a means of delivering drugs. According to Merriam Webster, the fact is that the term "transdermal" was introduced in 1944, signifying its novelty in medical and pharmaceutical fields. Transdermal medications come in self-contained, distinct dosage forms. Delivering drugs through the skin to produce a systemic impact without causing any variations in the drug's plasma levels. Administering therapeutic agents topically provides numerous benefits compared to traditional oral and invasive drug delivery techniques. Furthermore, it allows for the controlled release of the medication for a prolonged period of time. This review article briefly outlines the benefits and skin routes for transdermal drug delivery systems (TDDS), different parts of transdermal patch, and methods for creating transdermal patches. Assessment of transdermal systems, overall clinical factors in the use of TDDS, and restrictions of TDDS.*

Keywords: Transdermal, Permeation pathways, Drug delivery, Matrix, Reservoir

I. INTRODUCTION

Transdermal drug delivery systems (TDDS) are designed to deliver a therapeutic amount of medication through the skin of a patient, providing the necessary dose of the drug to the body. To achieve systemic effects through the skin for therapeutic substance delivery, it is crucial to thoroughly understand the biophysical, morphological, and physicochemical properties of the skin. Transdermal drug administration offers significant benefits over injections and oral methods by enhancing patient adherence and bypassing initial metabolism.⁽¹⁾

It guarantees a regulated and steady delivery of drugs, especially helpful for medications with quick biological half-lives, avoiding sudden introduction into the bloodstream that can cause negative side effects. Consequently, different advanced drug delivery systems, including Transdermal drug delivery systems, Transmucosal delivery systems, and Controlled release systems, have been created. Advantages of transdermal drug administration involve enhanced treatment efficacy, decreased liver metabolism, and sustaining a consistent drug level in the blood. The initial transdermal system received approval from the FDA in 1979 for the purpose of preventing nausea and vomiting. Confirmation of percutaneous drug absorption can be confirmed by measuring blood levels, detecting excretion of the drug and its metabolites in urine, and observing the patient's clinical response to the drug therapy administered.⁽²⁾

A specialized medicated patch called a transdermal patch is designed to deliver drugs into the bloodstream at a controlled rate by penetrating the skin layers. These patches provide a very convenient way to administer drugs, as they are painless and can offer continuous treatment for multiple days. Moreover, they can be easily stopped whenever necessary. Transdermal patches come in different sizes and may include several active ingredients. When these patches

are placed on the skin, they utilize diffusion mechanisms to transport the active ingredients directly into the bloodstream. Certain patches may have high concentrations of the active ingredient, which stays on the skin for a prolonged duration. The initial transdermal patch introduced in 1985 was Nitroglycerin, representing a notable advancement in drug delivery through the skin. Gale and Berggren created patches containing an ethylene vinyl acetate membrane that controls the release rate. Different medications come in the form of patches that are applied to the skin, including nicotine, estradiol, fentanyl, clonidine, scopolamine (hyoscine), and estradiol with norethisterone acetate. The location for applying the patch depends on the type of medication being used.⁽³⁾

For example, estradiol patches are usually placed in the vicinity of the buttocks or abdomen, whereas nitroglycerin patches can be put around the chest region. The length of time for drug release varies from 9 hours to 9 days, depending on the intended purpose.

ADVANTAGES

- Transdermal delivery prevents first-pass metabolism by providing a substance to permeate continuously and steadily over a long period of time.⁽⁴⁾
- Promote higher levels of patient adherence.⁽⁵⁾
- It does not disrupt the liquid in the stomach and intestines.⁽⁶⁾⁽⁷⁾
- Maintains consistent and steady blood levels, offering extended period control.
- Lower levels of drug concentration in the plasma.
- Minimize plasma level changes by using drugs with brief half-lives and narrow therapeutic indices.⁽⁸⁾
- If toxicity occurs, drug delivery can be quickly removed.
- Decreasing dosing frequency can improve patients' adherence.
- Transdermal administration improves the efficacy of many medications by avoiding specific problems associated with the drugs, like inadequate absorption and irritation in the gastrointestinal tract.
- The simplified drug regimen leads to less variation in drug reactions within and between patients.

DISADVANTAGES

- The drug needs to have good physicochemical properties in order to penetrate the stratum corneum.
- The drug amount should not exceed 5mg/day for daily doses; beyond 10-25 mg/day, transdermal drug delivery presents difficulties.
- The components in the patch, such as the medication, adhesive, and additional ingredients, may lead to local irritation.
- A definite clinical need must be outlined before using the transdermal delivery system.
- It was impossible to reach high levels of drugs in the blood/plasma.
- Drugs with a large molecular size are not able to be formulated.
- Chance of inflammation at the application site.⁽⁹⁾
- Uncomfortable to put on.
- May be uneconomical.
- The skin barrier differs among people and may also fluctuate in the same individual over time.

A BRIEF OVERVIEW OF TRANSDERMAL PATCHES/ITEMS AND THEIR DISTINGUISHING CHARACTERISTIC

Drugs	Indication	Product Name	Duration of Application	Reference
Asenapine	Mania, bipolar disorder	Secuado [®]	24 h	[9,10]
Bisoprolol	Atrial fibrillation	Bisono [®]	24 h	[11,12]
Buprenorphine	Management of pain	Butrans [®]	7 days	[13,14,15]

Drugs	Indication	Product Name	Duration of Application	Reference
Clonidine	Hypertension, Tic disorder, Tourette syndrome, Attention deficit hyperactivity disorder (ADHD)	Catapres-TTS [®]	7 days	[16,17,18,19]
Dextroamphetamine	ADHD	Xelstrym [®]	Up to 9 h	[20]
Donepezil	Alzheimer disease	Adlarity [®]	7 days	[21,22]
Estrogen	Postmenstrual syndrome	Fematrix [®]	7 days	[23,24]
Ethinyl Estradiol	Prevent pregnancy	Ortho Evra [®]	7 days	[25,26]
Fentanyl	Moderate/severe pain	Duragesic [®]	72 hours	[27]
Granisetron	Anti-emetic	Sancuso [®]	Up to 7 days	[28,29,30]
Levonorgestrel, Estradiol	Postmenstrual syndrome	Climara Pro [®]	7 days	[31,32]
Lidocaine	Treatment of pain	Lidoderm [®] , Dermalid [®]	up to 3 times daily for no more than 12 hours	[33,34]
Methylphenidate	ADHD	Daytrana [®]	Up to 9 days	[35]
Nicotine	Smoking cessation	Habitrol [®] , Nicoderm [®] , Nicoderm CQ [®] , Nicorette [®]	24 h 16 h	[36,37,38]
Nitroglycerin	Angina pectoris Relieve pain after surgery	Minitran [®] , Nitro-dur [®]	12–14 h	[39,40,41,42]
Norethindrone Estradiol	Symptoms of menopause	Combipatch [®]	3–4 days	[43]
Oxybutynin	Overactive bladder	Oxytrol [®]	3–4 days	[44,45]
Rivastigmine	Alzheimer disease	Exelon [®]	24 h	[46,47]
Rotigotine	Parkinson's disease	Neupro [®]	24 h	[48]
Selegiline	Depression	Emsam [®]	24 h	[49]
Scopolamine	Motion sickness	Transderm-scop [®]	72 h	[50,51]
Testosterone	Hypogonadism in males	Androderm [®]	24 h	[52,53]
17-β-Estradiol	Postmenstrual syndrome and osteoporosis	Alora [®] , Climara [®] , Estraderm [®] , Vivel-Dot [®] , Vivella [®]	3–4 days 7 days 3–4 days 3–4 days 3–4 days	[54,55,56]

Drugs	Indication	Product Name	Duration of Application	Reference
		Menostar®	7	days
		Minivelle®	3–4 days	

MECHANISM OF ACTION OF TRANSDERMAL PATCH

The application of the transdermal patch and the flow of the active drug constituent from the patch to the circulatory system via skin occur through various methods.

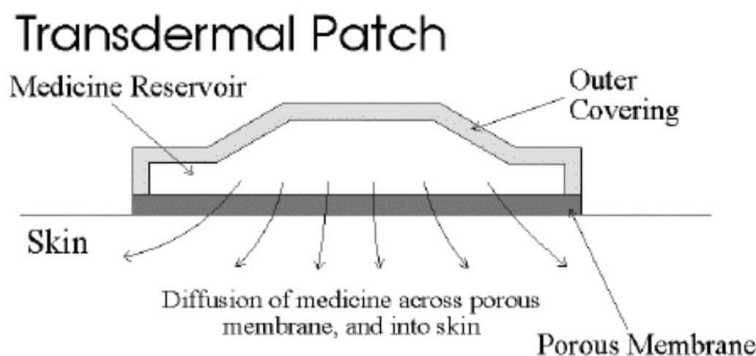


Figure 1

FUNCTIONS OF THE SKIN'S BIOLOGY:

The skin on a typical adult body spans a certain surface area about 2 square meters in size and gets around a third of the Blood moving throughout the body. Skin consists (figure 1) of a topmost layer called epidermis that contains different regions in terms of morphology; basal layer, spiny layer, stratum granulosum and outermost stratum corneum, it comprised of heavily keratinized (lifeless) cells trapped in a uninterrupted array of lipid layers. Terms and conditions apply to all purchases made on this platform. Extracellular membranes have distinctive compositions consist of ceramides, cholesterol, and free fatty acids chemical substances that release hydrogen ions when dissolved in water. Average, about 1 million bacteria per square centimeter. On average, there are 10 to 70 hair follicles and 200 to 250 sweat ducts each square centimeter of the skin's surface area. It is one of the utmost easily reached parts of the human body.^(57,58)

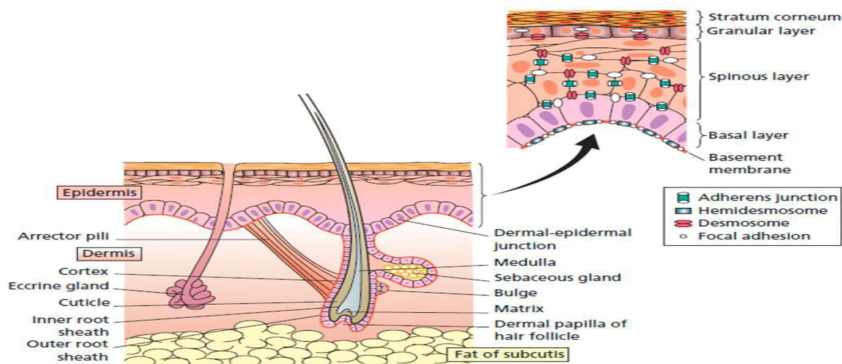


Figure 2: Anatomical and physiological Structure of skin

TRANSDERMAL DRUG DELIVERY THROUGH SKIN PATHWAYS

Penetration occurs when drugs are administered topically. Penetration and passage through the skin may happen through different pathways. Substances enter through the stratum corneum. Through the epidermis, or through the skin.

appendages (Figure 2) depicts. While moving through the stratum in the outer layer of the skin, two different paths can be identified. The penetration moves back and forth between the corneocytes/lipid lamellae (transcellular pathway) and ii) Infiltration through the winding path next to the lipid layers (between cells) path, way

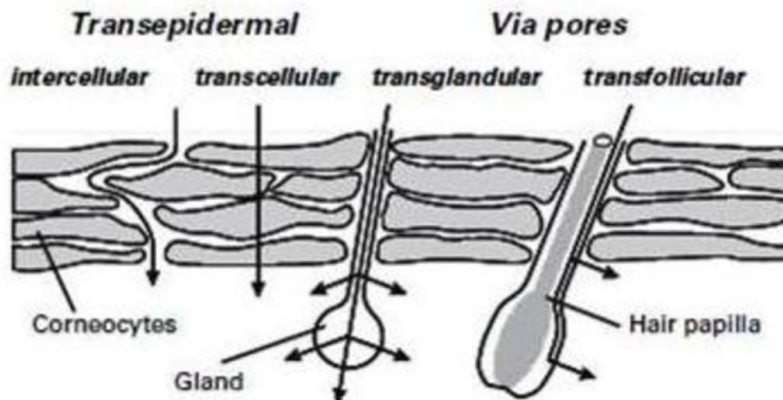


Figure 3: Potential routes for drug diffusion through the protective layer of skin

It is generally acknowledged that the main way of penetrating through the stratum corneum is the pathway between cells. This is predominantly the result of the high population density. Keratinocytes are covered by a cross-linked cornified envelope. Yet, transcellular movement of small hydrophilic substances. Substances like water cannot be entirely eliminated. The pathway via appendage or shunt involves the duct of the eccrine sweat glands or the follicular duct. The subtitle of the movie is "A Tale of Love and Loss". The primary composition of eccrine sweat glands is mostly water-loving. The follicular duct's content is lipophilic. This represents primarily because of the sebum produced in the entrance of the duct of the hair follicle. It is widely acknowledged that because of its substantial passive skin permeation, predominantly takes place on the surface area via unharmed outer layer of skin⁽⁵⁹⁻⁶²⁾

ESSENTIAL ELEMENTS OF TOPICAL ADMINISTRATION SYSTEMS FOR DELIVERING DRUGS:

- < Polymer material
- < Medication
- < Substances that increase permeability
- < Additional ingredients

Polymer matrix:

The polymer manages the dispensing of the drug from the device. For a polymer to be used in Transdermal devices, it must meet the specified criteria.

Table 1: Showing different types of polymers

Natural polymers	Synthetic Elastomers	Synthetic polymers
Cellulose derivatives, Zein, Gelatin, Waxes, Proteins, Gums, Natural rubber, Starch.	Polybutadiene, Hydrin rubber, polysiloxane, silicone rubber, Nitrile, Acrylonitrile, Butylrubber, Styrenebutadiene, Neoprene etc	Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyvinylpyrrolidone, Polymethyl methacrylate, Epoxy, Polyurea, etc.

Medication:

To achieve successful development of a transdermal drug delivery system. When selecting a drug, it is important to carefully consider the system it will interact with. The text must be paraphrased without changing the input language and keeping the word count the same. Here are a few of the desirable characteristics of a medication. Delivery through the skin

Characteristics of matter that relate to both physical and chemical aspects:

The medication needs to have a lower molecular weight less than about 1000 Daltons

The medication needs to exhibit a preference for both lipophilic substances and phases that are attracted to water

Intense division traits do not support effective medication transportation through the skin.

The medication must possess a low melting temperature.

Biological Properties:

The medication needs to be strong when taken once a day a few milligrams per day.

The drug's half life ($t_{1/2}$) should be brief.

The drug should not cause any irritation to the skin reaction to allergies.

Medications that break down in the gastrointestinal tract or become ineffective are appropriate choices for due to the hepatic first-pass effect.

Delivery through the skin Resistance to the medication should not build up over time.

Transdermal delivery exhibiting zero-order release pattern term, can have negative side effects on the body period during which negative impacts are provoked on non..

Target tissues can also be structured for transdermal delivery

Substances that increase permeability

Permeation enhancers or promoters are substances that do not have any direct pharmacological activity but help in increasing the absorption of drug have their own healing qualities but can also convey the absorption of medications from medication administration systems onto the Skin The movement of medications through the skin⁽¹¹⁾ can be expressed as:

$$J = D \frac{dc}{dx}$$

D, as the diffusion coefficient, varies with dimensions, form, and pliability of the dispersing molecule equally resistance of the membrane, with C representing the concentrations spreading substances; x represents the location dimension.

conditions is complex, it can be found by applying advanced mathematical techniques Variations in conditions and differences in membrane composition can cause significant differences sophisticated, the fundamental ideas concerning improvement in flux is present in the equation provided above The focus The origin of the gradient is thermodynamic, and it leads to diffusion Coefficient is connected to the dimensions and form of penetration the amount of energy needed to create an opening for diffusion In this way increasing the flow through membranes is reduced to factors to consider:

Thermodynamics involves lattice energies and distribution (factors) in the same quantity

Size and configuration at the molecular level.

Decreasing the energy needed for producing a molecular an opening in the membrane.

It is hypothesized that permeation enhancers have an impact on one To reach skin penetration, one or multiple layers must be penetrated Improvement Many compounds exist in abundance are searched for their potential to improve stratum permeability of the stratum corneum These conveniently organized.

Summarize the text

Restate the text clearly

Explain the text in a different way

Solvents: these substances could enhance penetration, potentially through

Increasing the polar routes within the skin.

Lipids becoming fluidized.

Some instances are water, along with alcohols like methanol and ethanol. methyl sulfoxides like dimethyl sulfoxide, alkyl compounds similar to methyl sulfoxide, dimethyl acetamide and dimethyl formamide; 2-pyrrolidones of pyrrolidone; Azone, also known as laurocapram, along with other solvents like propylene glycol, glycerol, fluids made from silicone, isopropyl palmitate.

Surfactant: These substances are suggested to improve transport through a polar pathway, particularly for hydrophilic medications A surfactant's capacity to change penetration is determined by its effectiveness of the length of the

hydrocarbon chain and the head group. These employees need to attend a mandatory training session next week. Compounds can irritate the skin, so achieving an equilibrium between improved penetration and irritation must be addressed. Pondered. Anionic surfactants have the ability to enter and engage with having a strong connection with the skin. Once these agents have entered the skin, they are capable of causing significant changes. It has been reported that cationic surfactants are more irritating than the rest. Anionic surfactants have not been extensively researched for improving absorption through the skin. There are three main categories of nonionic surfactants that have been known for a long time: those who are least likely to cause annoyance and have been extensively researched.

Various surfactants are commonly used.

Anionic Surfactants: Dioctyl sulphosuccinate, Sodium lauryl sulphate, Decyldecylmethyl sulphoxide etc.

Non Ionic Surfactants: Pluronic F127, Pluronic F68, etc.

Bile Salts: Sodium taurocholate, sodium deoxycholate, Sodium tauroglycocholate.

Miscellaneous chemicals: These include urea, a hydrating and keratolytic agent; N, N-dimethyl-m-toluamide; Calcium thioglycolate; Anticholinergic agents. Some potential permeation enhancers have recently been described but the available data on their effectiveness are sparse. These include eucalyptol, di-o-methyl-beta-cyclodextrin and soybean casein.

Other Excipients:

Adhesives: Securing transdermal devices in place is essential. Pressure-sensitive technology has been utilized to study skin up to this point. Sticky substance. The adhesive which is sensitive to pressure can be located on the front or back of the device equipment and expanding outward.

Both adhesive systems should fulfill the following criteria

Must not inflame or cause sensitivity to the skin. Lack of balance in the typical skin microbiota.

Must stick firmly to the skin during the process dosing frequency without being disrupted by its placement tasks like washing, physical activity, etc.

Should be easily removed

Must not leave a residue on the skin that cannot be washed off.

Must have outstanding (close) connection with the skin at both the macro and micro level.

Backing Membrane: Backing membranes are pliable and adaptable. They create a strong connection with the drug reservoir, stopping prevent the drug from exiting the dosage form via the upper area. Authorize to proceed with printing. It is impenetrable and provides protection for the product while being used on the skin such as metallic plastic laminate or plastic supporting with a pad that absorbs and a sealing base plate flexible adhesive foam pad made of aluminum foil. Polyurethane material with a sealing base plate made of aluminum foil disc.

Release Liner: Storage is facilitated by the presence of a release liner. Loss of the drug that has moved into the sticky layer and pollution. It is thus considered to be a component of the primary packaging material instead of being a component of the dose method for administering the medication. The protective backing is made up of a primary layer that could be breathable (paper cloth) or an obstructive (polyethylene, polyvinylchloride) and a coating layer made of either silicon or Teflon for releasing. Alternatively Polyester is one of the materials commonly used in the release liner for TDDS. Metallic foil and laminated metal film.

TYPES OF TRANSDERMAL PATCHES

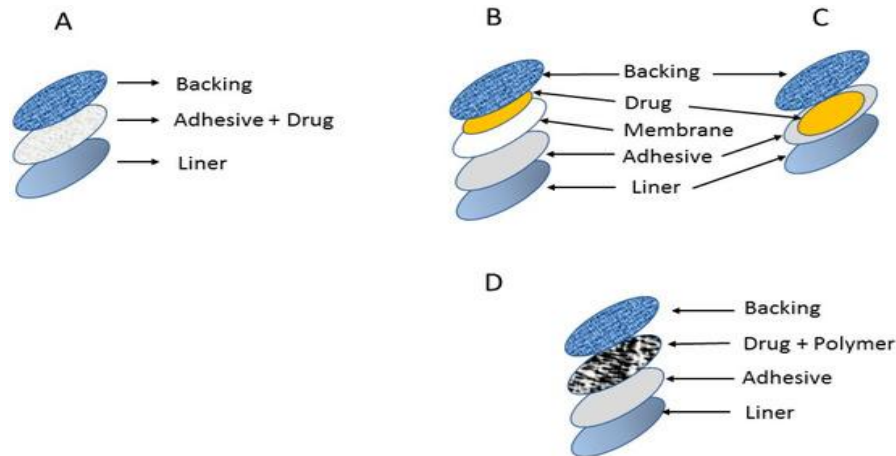


Figure 4

Transdermal patches are classified based on their design, functionality, and therapeutic applications. Here are some common types of transdermal patches:

1 Matrix-type patches:

- Contain drug reservoir surrounded by polymer matrix
- Drug diffuses through matrix to skin
- Examples: nicotine, fentanyl, and estradiol patches

2 Reservoir-type patches:

- Separate drug reservoir and adhesive layer
- Drug diffuses through rate-controlling membrane
- Examples: scopolamine and clonidine patches

3 Adhesive-type patches:

- Drug dispersed directly in adhesive
- No separate reservoir or matrix
- Examples: lidocaine and capsaicin patches

4 Ionophoretic patches:

- Use low electrical current to enhance drug delivery
- Examples: lidocaine and fentanyl patches for pain management

5 Electroporation patches:

- Use high-voltage pulses to create temporary skin pores
- Enhance drug delivery and vaccination efficacy

6 Microneedle patches:

- Use tiny needles to create micro-channels in skin
- Increase drug absorption and reduce invasiveness

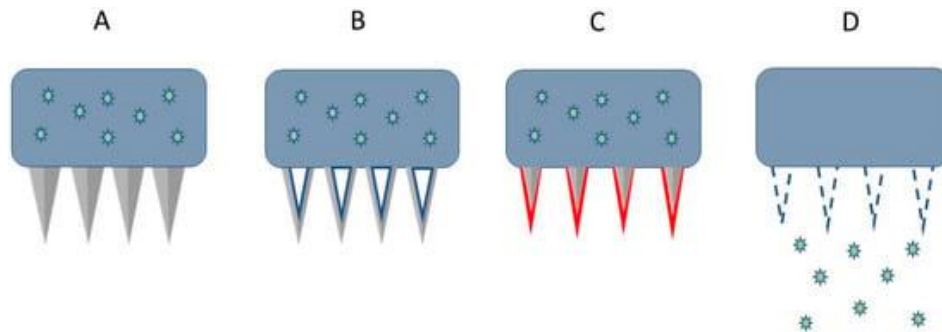


Figure 5: The microneedle-based patch
(A) solid; (B) hollow; (C) coated; (D) dissolving.

7 Thermal patches:

- Use heat to enhance drug delivery and skin permeability
- Examples: heat-activated lidocaine patches

8 Ultrasound patches:

- Use low-frequency ultrasound to enhance drug delivery
- Examples: ultrasound-mediated insulin delivery

Therapeutic Applications:

- 1 Pain management (e.g., lidocaine, fentanyl)
- 2 Smoking cessation (e.g., nicotine)
- 3 Hormone replacement therapy (e.g., estradiol)
- 4 Cardiovascular disease (e.g., clonidine)
- 5 Neurological disorders (e.g., rivastigmine)
- 6 Motion sickness (e.g., scopolamine)
- 7 Local anesthesia (e.g., lidocaine)
- 8 Vaccination (e.g., influenza, COVID-19)

RECENT ADVANCEMENT OF TRANSDERMAL PATCH

Conventional transdermal patches have two primary functions: storing drugs and releasing them. Despite its benefits, traditional patching poses several obstacles and disadvantages, such as restricted dosage or minimal release. Until now, there have been various improvements in transdermal drug delivery. These features consist of new patch designs with improved drug sensing and release capabilities, increased drug loading, and improved drug penetration and release. In general, transdermal drug delivery is a lively area of research and development, with numerous promising new advancements on the way, as detailed later in this discussion.

Smart patches

Dissolving/Degradable patches

Three-Dimensional (3D)-Printed Patches

High Loading/Release Patches

Potential Application of Transdermal Patches

Transdermal Patches for Vaccination

Transdermal Patches for Gene Therapy

Transdermal Patches for Insulin Delivery

Transdermal Patches for Cardiovascular Diseases

Transdermal Patches for hormonal Deficiencies and Contraception

Transdermal Patches for Central Nervus System (CNS) Disorder

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Transdermal Patches for Infectious Diseases.

CONDITION IN WHICH TRANSDERMAL PATCHES ARE USED:

Transdermal patch is used when:

- When the patient has intolerable side effects (including constipation) and who is unable to take oral medication and is requesting an alternative method of drug delivery.
- Where the pain control might be improved by reliable administration this might be useful in patient with cognitive impairment or those who for other reason are not able to self-medicate with their analgesia.

CONDITION IN WHICH TRANSDERMAL PATCHES ARE NOT USED:

The use of transdermal patch is not suitable when:

- Cure for acute pain is required
- Where rapid dose titration is required
- Where requirement of dose is equal to or less than 30 mg/24hrs.

PREPARATION OF TRANSDERMAL PATCHES

Transdermal drug delivery patches can be prepared by various methods

Mercury Substrate Method:

This technique involves dissolving the necessary drug quantity predefined quantity of polymer solution together with Substance used to soften or increase the flexibility of plastic Mix the solution above for a while adequate time is required to create a uniform mixture and maintain it set aside until all air bubbles are completely removed before continuing poured into a glass ring positioned above the mercury A glass petri dish with a smooth top The speed at which evaporation occurs controlling the solvent is done by covering it with an upside-down funnel container for growing microorganisms The desiccator is where the dried films should be stored⁽⁶³⁻⁶⁷⁾

Circular Teflon Mould Method:

Polymers of different proportions are present in solutions frequently utilized in a solvent of organic origin The quantity of drug is measured and mixed in liquid form in half the amount of the identical organic solvent Softening agent incorporated into polymer solution for drugs The complete contents need to be accounted for Get mixed and subsequently transferred into a round Teflon container Solvent vaporization rate is regulated by placement Glass funnel inverted onto Teflon mold The substance used for dissolving is permitted to dry out for 24 hours The dried coatings need to be kept in a desiccator⁽⁶⁸⁾

Glass Substrate Method:

The polymeric solutions are set aside to swell The necessary amount of plasticizer and drug solution is included and agitated for 10 minutes Additionally, it is designated for certain purposes The time needed to remove any trapped air is taken before pouring the Sanitize and ensure a petri dish is free of moisture The solvent rate controlling evaporation by placing a glass funnel upside down over the dish used in laboratories for culturing microorganisms The dried films are removed the next day removed and kept in a dehydration chamber⁽⁶⁹⁾

By Using IPM Membrane 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⁽⁷⁰⁾.

By Using EVAC Membranes Method:

To get ready for the intended transdermal treatment gel reservoir with 1% carbopol system, polyethylene (PE) EVAC membranes, consisting of ethylene vinyl acetate copolymer, are able to serve as membranes for controlling rates. If the medication is not Propylene glycol, which can be dissolved in water, is utilized for the same purposes. Making gel medicine is mixed into propylene glycol carbopol resin is to be included in the solution mentioned above. Neutralization is achieved through the use of a 5% weight/weight solution of sodium hydroxide. The gel form of the drug is applied onto a backing sheet. A covering layer that spans the designated region. A controlling rate a membrane will cover the gel and the edges will be secured/locked through heat to achieve a device that is resistant to leaks.⁽⁷¹⁾

Aluminium Backed Adhesive Film Method

Transdermal drug delivery system has the potential to create unpredictable outcomes/matrices when the initial dose exceeds 10 mg. The aluminum-backed adhesive film technique is an appropriate option. Chloroform is the preferred solvent for preparing the same since the majority of drugs and adhesive can dissolve in a solution of chloroform. The chloroform dissolves the drug. The drug solution will have adhesive material added to it/broken down. An aluminum former customized specifically for the task is coated with aluminum foil with the edges sealed tightly/cork cube.⁽⁷²⁾

Asymmetric TPX Membrane Method

A model patch can be created using a heat-sealing method/polyester film (1009 type, 3m) with a curvature of 1cm diameter serves as the supporting membrane. Sample of medication is provided/poured into the curved surface, protected by a TPX film. Asymmetrical membrane made of poly(4-methyl-1-pentene) secured by a sticky substance.⁽⁷³⁾

EVALUATION IN TEST OF TRANSDERMAL PATCH

Drug Excipients Interaction Studies:

The drug must be compatible with excipients to create an effective medication. It is essential to identify any potential issues with the product to ensure its stability/interaction involving both physical and chemical elements. Studies examining interactions are conducted. Frequently conducted using thermal analysis, FT-IR analyzing studies using UV and chromatographic methods/their chemical and physical properties like testing, liquefying Warm-blooded animals, specific frequencies, and uptake maximum and so on.

Water Vapor Transmission Rate (WVTR) Studies: Glass vials of the same size were utilized for transmission. The building blocks of all living organisms are cells. These transmission cells were cleaned completely/then heated in oven at 100 oC for a period of time. Approximately one gram cells were filled with anhydrous calcium chloride. The polymer film of each was attached to the edge. The cell structure is made up of various components/were precisely measured and stored in a sealed desiccator holding a saturated potassium chloride solution within. Water Vapor Transmission Rate = $\frac{\text{Final Weight} - \text{Initial Weight}}{\text{Time} \times \text{Area}}$. It is expressed as the number of grams of moisture gained/hr/cm.sq.

Thickness of the patch: The drug loaded's thickness. A digital is used to measure the patch at various points/measures in micrometers to calculate the mean thickness/standard deviation to guarantee consistency in thickness.

Skin Irritation Study: Irritation and sensitization of the skin. Healthy rabbits can undergo testing (average weight 1.2 to 1.5 kg). The upper side of the rabbit is to be cleaned and have its hair removed/prepare the dorsal surface by shaving and cleansing the area. Rectified alcohol and the typical compositions may be utilized/placed on the skin. The patch should be taken off in 24 hours. The skin should be monitored and categorized into 5 categories every few hours/grading according to the seriousness of the skin damage.

Flatness Test: Three vertical strips are going to be removed from each movie is positioned at a distinct location, such as one being in the middle/one from the left side and another from the right edge. Measure the length of each strip/difference in size due to unevenness in flatness/constriction was assessed by calculating the percentage of constriction. 0% restriction is the same as 100% flatness.

Drug content: A particular section of the patch must be designated mixed in an appropriate liquid in a particular amount. Next, the answer must pass through a filtering substance and analyze the drug composition using the appropriate technique (UV or) Technique of HPLC. Every value is the average of three Examples.

Weight Uniformity: The patches that have been prepared need to be dried. Testing will take place after the sample has been kept at a temperature of 60°C for a duration of 4 hours. A designated patch of land is meant to be sliced into various sections of the area and then measured in terms of weight electronic scale. The mean weight and deviation is standard. Calculations will be done based on the weights of each individual.

Folding Endurance: A piece of particular size needs to be sliced. Folded in a uniform manner at a consistent location until it eventually fractured. The film could be folded the same number of times position without tearing provided the worth of the bending endurance.

Swellability: The 3.14 cm² patches were measured in weight place into a petri dish with 10 ml of double distilled water and were permitted to drink. Weight gain has occurred the patch was scheduled to be applied at specific time intervals, up to a certain point consistent weight was noted.

The degree of swelling (S) was calculated using the formula,

$$S (\%) = \frac{W_t - W_0}{W_0} \times 100$$

Where S is percent swelling

W_t is the weight of patch at time t and W₀ is the weight of patch at time zero.

Moisture Loss: The films that are ready need to be measured separately and stored in a desiccator with appropriate care calcium chloride at a temperature of 40 degrees Celsius. The films should be left for 24 hours reassessed and calculated the amount of moisture lost as a percentage from the formula below

$$\% \text{ Moisture Loss} = \left[\frac{\text{Initial wt} - \text{Final wt}}{\text{Final wt}} \right] \times 100$$

Percentage Moisture Uptake: The films that were measured have to be analyzed. Place in desiccators at room temperature for 24 hours holding a fully saturated potassium chloride solution within in order to keep RH at 84%. The films should be watched within 24 hours weighed again to establish the moisture uptake percentage from the formula provided below.

Probe Tack Test: Weight is measured using a scale with units in grams. During this examination, the point of a sterile probe was used a specified level of roughness is put in touch with sticky and when the probe is attached sticky substance. The probe was then removed breaks it in a mechanical way. The amount of force needed to drag the object investigating the adhesive by moving away at a constant speed is noted. Weight is measured in grams.

Percentage Elongation Break Test: The proportion The length must be observed to determine elongation break right before the breaking point, there is an increase in the percentage of extension can be calculated using the formula provided below.

Tensile Strength: A modified pulley system is utilized to study the tensile strength of the file. The system measures the force needed to break the film, providing valuable information about its tensile strength.

Shear adhesion test: This test is conducted to assess the cohesive strength of the adhesive polymer. In this method, the adhesive-coated patch is applied over a smooth surface, and a specific weight is hung from the patch parallel to the surface. The duration taken to pull off the patch from the surface measures its shear adhesion property, indicating the strength of the adhesive bond.

Peel adhesion test: In this test, the force required to remove the patch from a surface is determined. The patch is applied to a steel plate, and then it is pulled away at a 180-degree angle from the surface. The force needed to detach the patch is measured, providing information about its adhesive strength.

Rolling ball tack test: In this test, a steel ball with a diameter of 7/16 inch is rolled down on inclined plane with the horizontally placed patch facing upward, adhesive surface exposed. The ball rolls down and travels a specific horizontal distance on the patch. The distance covered by the ball provides information about the tackiness or tack property of the adhesive patch. Tackiness is an adhesive's ability to quickly adhere to a surface upon contact.

Thumb tack test: Tackiness is determined by the force needed to separate a thumb or any object from an adhesive surface.

In-vitro drug release studies: The disk on top of the paddle USP apparatus V method can be used for evaluation of the drug's dissemination from the fabricated patches of land. The plan is to cut dry films of a specified thickness exact form, measured and secured onto a glass surface with a sticky substance. The glass plate was subsequently inserted into a 500-ml container of the solution medium or phosphate buffer at a pH of 7.4. Equipment was adjusted to a temperature of $32 \pm 0.5^\circ\text{C}$. The paddle was later positioned 2.5 cm away from the glass plate spinning at a rate of 50 revolutions per minute. 5 milliliters of samples. Fractions can be taken out at the right intervals for 24 hours and tested using a UV spectrophotometer or high-tech analysis machine high performance liquid chromatography (HPLC) technology. The text needs to be provided in order to be paraphrased. An experiment will be conducted three times and the average will be calculated. Calculating value is possible.

In-vivo studies: The genuine representation comes from in-vivo assessments regarding the drug's effectiveness. The variables that are unable to be fully considered in in-vitro studies investigated through in-vivo experiments. Assessment of in vivo conditions TDDS can be performed by utilizing:

Models of animals

Volunteers who are human

Stability Studies: Experiments on stability are to be carried out based on the ICH guidelines through storing the TDDS samples stored at a temperature of $40 \pm 0.5^\circ\text{C}$ and a relative humidity of $75 \pm 5\%$ for a period of 6 months. Text should be paraphrased while maintaining the same vocabulary and word counts. Samples were taken at intervals of 0, 30, 60, 90, and 180 days. Examine appropriately for the medication's ingredients.

LIMITATIONS FOR SELECTION OF TDDS

Not all drugs can be given using this method/pathway; the drug needs to possess certain favorable Physico-Chemical characteristics.

Unsuitable for medications that necessitate elevated plasma concentrations.

Inappropriate for medications causing skin irritation/dermatitis caused by contact.

Inappropriate for medications with large molecular size.

Inappropriate for medications that experience metabolism while undergoing treatment/the penetration of the skin.

II. CONCLUSION AND UPCOMING OBSTACLES

Effective way to administer medication through the skin a possible method to provide consistent administrations of numerous drugs. A variety of medications can be administered. Enhanced drug absorption with minimal adverse effects and complications. Advantages include affordability and simplicity of use. A decade earlier, smoking cessation had been revolutionized by the nicotine patch. Patients were undergoing treatment with nitroglycerin for angina. Clonidine is used to treat high blood pressure, while scopolamine is for motion sickness. Illness and estradiol for lack of estrogen, throughout patches are utilized by more than one million patients annually. The current method for delivering a drug product is through transdermal means. Approved in the form of oral dosage, enables the prevention of metabolism that occurs

during the initial passage through the body effective method for delivering medication through the skin, providing consistent and controlled absorption. A popular way to administer drugs through the skin. Nevertheless, the limitations of transdermal technologies are caused by a fairly resistant layer of thick outer stratum corneum. Scientists are working to overcome this obstacle. Inadequate permeability due to physical and chemical factors.

Recently, there have been numerous advancements in transdermal patch technology, such as the creation of intelligent, dissolvable/biodegradable, high-capacity/release, and 3D-printed patches. Despite the potential benefits of transdermal patches for drug delivery, challenges including self-inflicted toxicity from incorrect dosing, poor adhesion, low drug penetration, skin irritation, and patch failure must be addressed. Further research and development are necessary to enhance the safety and effectiveness of this delivery system.

REFERENCES

- [1]. LV Allen NG Popovich C Howard Ansel Pharmaceutical dosage forms and drug delivery systems, 8th Edn. Wolter Kluwer Publishers New Delhi 2005 2989
- [2]. P Kumar C Sankar B Mishra Delivery of macromolecules through skin Indian Pharm 2004 53 717
- [3]. OA Al Hanbali HMS Khan M Sarfraz M Arafat S Ijaz A Hameed Transdermal patches: Design and current approaches to painless drug delivery Acta Pharm 2019 69 219 715
- [4]. Y Zhang J Yu AR Kahkoska J Wang J B Buse Z Gu Advances in transdermal insulin delivery Adv Drug Deliv Rev 2019 139 517 010.1016/j.addr.2018.12.006
- [5]. P De Vos MM Faas M Spasojevic J Sikkema Encapsulation for preservation of functionality and targeted delivery of bioactive food components Int Dairy J 2010 20 429 2302
- [6]. P Heifer TR Shultz Coupled feedback loops maintain synaptic long-term potentiation: A computational model of PKMzeta synthesis and AMPA receptor trafficking PLoS Comput Biol 2018 14 510061 4710.1371/journal.pcbi.1006147
- [7]. B Barry EM Aulton Transdermal drug delivery The science of dosage forms design, 2nd edn. Harcourt publishers Churchill Livingstone, New York 2002 499 533
- [8]. AC Williams BW Barry Penetration enhancers Adv Drug Deliv Rev 2012 64 512 818
- [9]. Musselman M., Faden J., Citrome LA. Aripiprazole: An atypical antipsychotic with atypical formulations *Ther Adv Psychopharmacol* 2021;11:20451253211035269 doi: 10.1177/20451253211035269 [PM C free article] [PubMed] [CrossRef] [Google Scholar]
- [10]. Musselman M., Faden J., Citrome LA. Aripiprazole: An atypical antipsychotic with atypical formulations *Ther Adv Psychopharmacol* 2021;11:20451253211035269 doi: 10.1177/20451253211035269 [PM C free article] [PubMed] [CrossRef] [Google Scholar]
- [11]. Yamashita T., Ikeda T., Akita Y. Comparison of heart rate reduction effect and safety between bisoprolol transdermal patch and bisoprolol fumarate oral formulation in Japanese patients with persistent/permanent atrial fibrillation (BISONO-AF study) *J Cardiol* 2019;73:386–393 doi: 10.1016/j.jcc.2018.11.009 [PubMed] [CrossRef] [Google Scholar]
- [12]. Transdermal buprenorphine (Butrans) for chronic pain *Med Lett Drugs Ther* 2011;53:31–32 [PubMed] [Google Scholar]
- [13]. James I.G., O'Brien C.M., McDonald C. A randomized, double-blind, double-dummy comparison of the efficacy and tolerability of low-dose transdermal buprenorphine (BuTrans seven-day patches) with buprenorphine sublingual tablets (Temgesic) in patients with osteoarthritis pain *J Pain Symptom Manag* 2010;40:266–278 doi: 10.1016/j.jpainsymman.2010.01.013 [PubMed] [CrossRef] [Google Scholar]
- [14]. Smyth M., Haupt T.S., Gregoire M.C. Retrospective Review of the Use of Transdermal Buprenorphine Patches (Butrans) in a Pediatric Population *J Palliat Med* 2020;23:1094–1097 doi: 10.1089/jpm.2019.0381 [PubMed] [CrossRef] [Google Scholar]
- [15]. Guo J.M., Shi X.X., Yang S.W., Qian Q.F., Huang Y., Xie Y.Q., Ou P. Efficacy of clonidine transdermal patch in treatment of moderate to severe tic disorders in children *Chin J Contemp Pediatr* 2017;19:786–789 doi: 10.7499/j.issn.1008-8830.2017.07.011 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

- [16]. Kang H., Zhang Y.F., Jiao F.Y., Guo X.Y., Gao X.M. Efficacy of clonidine transdermal patch for treatment of Tourette's syndrome in children *Chin J Contemp Pediatr* 2009;11:537–539 [PubMed] [Google Scholar]
- [17]. Ke G.M., Wang L., Xue H.Y., Lu W.L., Zhang X., Zhang Q., Guo H.Y. In vitro and in vivo characterization of a newly developed clonidine transdermal patch for treatment of attention deficit hyperactivity disorder in children *Biol Pharm Bull* 2005;28:305–310 doi: 10.1248/bpb.28.305 [PubMed] [CrossRef] [Google Scholar]
- [18]. Song P.P., Jiang L., Li X.J., Hong S.Q., Li S.Z., Hu Y. The Efficacy and Tolerability of the Clonidine Transdermal Patch in the Treatment for Children with Tic Disorders: A Prospective, Open, Single-Group, Self-Controlled Study *Front Neuro* 2017;8:32 doi: 10.3389/fneur.2017.00032 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [19]. Antihypertensive Patch Italian Study (APIS) Investigators One year efficacy and tolerability of clonidine administered by the transdermal route in patients with mild to moderate essential hypertension—A multicentre open label study *Clin Auton Res* 1993;3:379–383 doi: 10.1007/BF01829457 [PubMed] [CrossRef] [Google]
- [20]. Cutler A.J., Suzuki K., Starling B., Balakrishnan K., Komaroff M., Castelli M., Meeves S., Childress A.C. Efficacy and safety of dextroamphetamine transdermal system for the treatment of attention-deficit/hyperactivity disorder in children and adolescents: Results from a pivotal phase 2 study *J Child Adolesc Psychopharmacol* 2022;32:89 doi: 10.1089/cap.2021.0107 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [21]. Kim Y.H., Choi H.Y., Lim H.S., Lee S.H., Jeon H.S., Hong D., Kim S.S., Choi Y.K., Bae K.S. Single dose pharmacokinetics of the novel transdermal donepezil patch in healthy volunteers *Drug Des Dev Ther* 2015;9:1419–1426 doi: 10.2147/DDDT.S78555 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [22]. Yoon S.K., Bae K.S., Hong D.H., Kim S.S., Choi Y.K., Lim H.S. Pharmacokinetic evaluation by modeling and simulation analysis of a donepezil patch formulation in healthy male volunteers *Drug Des Devel Ther* 2020;14:1729 doi: 10.2147/DDDT.S244957 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [23]. Aguirre W., Chedraui P., Mendoza J., Ruilova I. Gabapentin vs low-dose transdermal estradiol for treating post-menopausal women with moderate to very severe hot flashes *Gynecol Endocrinol* 2010;26:333–337 doi: 10.3109/09513590903511539 [PubMed] [CrossRef] [Google Scholar]
- [24]. Clemente C., Caruso M.G., Berloco P., Buonsante A., Giannandrea B., Di Leo A. Alpha-Tocopherol and beta-carotene serum levels in post-menopausal women treated with transdermal estradiol and oral medroxyprogesterone acetate *Horm Metab Res* 1996;28:558–561 doi: 10.1055/s-2007-979852 [PubMed] [CrossRef] [Google Scholar]
- [25]. Ziemann M. The introduction of a transdermal hormonal contraceptive (Ortho Evra/Evra) *Fertil Steril* 2002;77:S1–S2 doi: 10.1016/S0015-0282(01)03274-5 [PubMed] [CrossRef] [Google Scholar]
- [26]. Ziemann M., Guillebaud J., Weisberg E., Shangold G.A., Fisher A.C., Creasy G.W. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: The analysis of pooled data *Fertil Steril* 2002;77:S13–S18 doi: 10.1016/S0015-0282(01)03275-7 [PubMed] [CrossRef] [Google Scholar]
- [27]. Baumrucker S.J. Duragesic (transdermal fentanyl) in hospice care *Am J Hosp Palliat Care* 1996;13:13–15 doi: 10.1177/104990919601300608 [PubMed] [CrossRef] [Google Scholar]
- [28]. Abramowicz M., Zuccotti G., Pflomm J.M., Daron S.M., Houst B.M., Zanone C.E., Dalton V.K., Epstein E.J., Hirsch J., Juurlink D.N.A. granisetron patch (sancuso) *Med Lett Drugs Ther* 2008;50:103–104; quiz p102 following 104 [PubMed] [Google Scholar]
- [29]. Howell J., Smeets J., Drenth H.J., Gill D. Pharmacokinetics of a granisetron transdermal system for the treatment of chemotherapy-induced nausea and vomiting *J Oncol Pharm Pract* 2009;15:223–231 doi: 10.1177/1078155209104063 [PubMed] [CrossRef] [Google Scholar]
- [30]. Le T.N., Adler M.T., Ouillette H., Berens P., Smith J.A. Observational Case Series Evaluation of the Granisetron Transdermal Patch System (Sancuso) for the Management of Nausea/Vomiting of

- Pregnancy *AmJP Perinatol* 2017;34:851–855 doi: 10.1055/s-0037-1598652 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [31]. Badoi D., Crauciuc E., Rusu L., Luca V. Therapy with climara in surgical menopause *RevMedChirSocMedNatIasi* 2012;116:828–833 [[PubMed](#)] [[Google Scholar](#)]
- [32]. Taggart W., Dandekar K., Ellman H., Notelovitz M. The effect of site of application on the transcutaneous absorption of 17-beta estradiol from a transdermal delivery system (Climara) *Menopause* 2000;7:364–369 doi: 10.1097/00042192-200007050-00010 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [33]. Desai M.J., Siriki R., Wang D. Treatment of pain in Dercum's disease with Lidoderm (lidocaine 5% patch): A case report *Pain Med* 2008;9:1224–1226 doi: 10.1111/j.1526-4637.2008.00417.x [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [34]. Karmarkar A., Lieberman I. Management of complex regional pain syndrome type II using lidoderm 5% patches *BrJ Anaesth* 2007;98:261–262 doi: 10.1093/bja/ael343 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [35]. Wokovich A.M., Shen M., Doub W.H., Machado S.G., Buhse L.F. Evaluating elevated release liner adhesion of a transdermal drug delivery system (TDDS): A study of Daytrana methylphenidate transdermal system *Drug Dev Ind Pharm* 2011;37:1217–1224 doi: 10.3109/03639045.2011.565773 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [36]. Chen H.K., Lan T.H., Wu B.J. A double-blind randomized clinical trial of different doses of transdermal nicotine patch for smoking reduction and cessation in long-term hospitalized schizophrenic patients *Eur Arch Psychiatry Clin Neurosci* 2013;263:75–82 doi: 10.1007/s00406-012-0338-3 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [37]. Perng R.P., Hsieh W.C., Chen Y.M., Lu C.C., Chiang S.J. Randomized, double-blind, placebo-controlled study of transdermal nicotine patch for smoking cessation *J Formos Med Assoc* 1998;97:547–551 [[PubMed](#)] [[Google Scholar](#)]
- [38]. Rich J.D. Transdermal nicotine patch for smoking cessation *NEngl J Med* 1992;326:344–345 [[PubMed](#)] [[Google Scholar](#)]
- [39]. Dahlstrom C.G., Rasmussen K., Bagger J.P., Henningsen P., Haghfelt T. Transdermal nitroglycerin (Transiderm-Nitro) in the treatment of unstable angina pectoris *Dan Med Bull* 1986;33:265–267 [[PubMed](#)] [[Google Scholar](#)]
- [40]. Greco R., D'Alterio D., Schiattarella M., Boccia A., Greco L., Marsico F. Efficacy of a new transdermal nitroglycerin patch (Deponit 10) for stable angina pectoris *Am J Cardiol* 1988;61:44E–51E doi: 10.1016/0002-9149(88)90090-2 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [41]. Mammen M.V., Tripathi M., Chandola H.C., Tyagi A., Bais P.S., Sanjeev O.P. Comparison of Enhancement of Analgesic Effect of Intrathecal Neostigmine by Intrathecal Clonidine and Transdermal Nitroglycerin Patch on Bupivacaine Spinal Anesthesia *Anesth Essays Res* 2017;11:993–997 doi: 10.4103/aer.AER_68_17 [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [42]. Savonitto S., Motolese M., Agabiti-Rosei E. Antianginal effect of transdermal nitroglycerin and oral nitrates given for 24 hours a day in 2,456 patients with stable angina pectoris: The Italian Multicenter Study *Int J Clin Pharmacol Ther* 1995;33:194–203 [[PubMed](#)] [[Google Scholar](#)]
- [43]. Archer D.F., Furst K., Tipping D., Dain M.P., Vandepol CA. Randomized comparison of continuous combined transdermal delivery of estradiol-norethindrone acetate and estradiol alone for menopause: CombiPatch Study Group *Obstet Gynecol* 1999;94:498–503 doi: 10.1016/s0029-7844(99)00359-2 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [44]. Dull P. Transdermal oxybutynin (oxytrol) for urinary incontinence *Am Fam Physician* 2004;70:2351–2352 [[PubMed](#)] [[Google Scholar](#)]
- [45]. Ho C. Transdermally-delivered oxybutynin (Oxytrol(R)) for overactive bladder *Issues Emerg Health Technol* 2001;24:1–4 [[PubMed](#)] [[Google Scholar](#)]
- [46]. Kurz A., Farlow M., Lefevre G. Pharmacokinetics of a novel transdermal rivastigmine patch for the treatment of Alzheimer's disease: A review *Int J Clin Pract* 2009;63:799–805 doi: 10.1111/j.1742-1241.2009.02052.x [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]

- [47]. Lefevre G., Pommier F., Sedek G., Allison M., Huang H.L., Kiese B., Ho Y.Y., Appel-Dingemans S. Pharmacokinetics and bioavailability of the novel rivastigmine transdermal patch versus rivastigmine oral solution in healthy elderly subjects *J Clin Pharmacol* 2008;48:246–252 doi: 10.1177/0091270007312154 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [48]. Chatsis V. Rotigotine transdermal patches (Neupro) for the treatment of Parkinson's disease *Issues Emerg Health Technol* 2008;112:1–6 [[PubMed](#)] [[Google Scholar](#)]
- [49]. Jessen L., Kovalick L.J., Azzaro A. The selegiline transdermal system (emsam): A therapeutic option for the treatment of major depressive disorder *P T Peer-Rev J Formul Manag* 2008;33:212–246 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- [50]. Johnson P., Hansen D., Matarazzo D., Petterson L., Swisher C., Trappolini A. Transderm Scop for prevention of motion sickness *N Engl J Med* 1984;311:468–469 doi: 10.1056/NEJM198408163110713 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [51]. Swaminathan S.K., Strasinger C., Kelchen M., Carr J., Ye W., Wokovich A., Ghosh P., Rajagopal S., Ueda K., Fisher J., et al. Determination of Rate and Extent of Scopolamine Release from Transderm Scop(R) Transdermal Drug Delivery Systems in Healthy Human Adults *AAPS PharmSciTech* 2020;21:117 doi: 10.1208/s12249-020-01658-4 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [52]. Bhasin S., Storer T.W., Asbel-Sethi N., Kilbourne A., Hays R., Sinha-Hikim I., Shen R., Arver S., Beall G. Effects of testosterone replacement with a nongenital, transdermal system, Androderm, in human immunodeficiency virus-infected men with low testosterone levels *J Clin Endocrinol Metab* 1998;83:3155–3162 doi: 10.1210/jc.83.9.3155 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [53]. De Sanctis V., Vullo C., Urso L., Rigolin F., Cavallini A., Caramelli K., Daugherty C., Mazer N. Clinical experience using the Androderm testosterone transdermal system in hypogonadal adolescents and young men with beta-thalassemia major *J Pediatr Endocrinol Metab* 1998;11((Suppl3)):891–900 [[PubMed](#)] [[Google Scholar](#)]
- [54]. Buch A., Shen L., Kelly S., Sahota R., Brezovic C., Bixler C., Powell J. Steady-state bioavailability of estradiol from two matrix transdermal delivery systems, Alora and Climara *Menopause* 1998;5:107–112 doi: 10.1097/00042192-199805020-00009 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [55]. Rozenbaum H., Birkhauser M., De Nooyer C., Lambotte R., Pornel B., Schneider H., Studd J. Comparison of two estradiol transdermal systems (Oesclim 50 and Estraderm TTS 50) I. Tolerability, adhesion and efficacy *Maturitas* 1996;25:161–173 doi: 10.1016/S0378-5122(96)01068-7 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [56]. Youngkin E. Q. Estrogen replacement therapy and the estraderm transdermal system *Nurse Pract* 1990;15:19–26, 31 doi: 10.1097/00006205-199005000-00005 [[PubMed](#)] [[CrossRef](#)] [[Google Scholar](#)]
- [57]. Yie W, Chien, Novel Drug Delivery Systems, 2nd ed, M Dekker, 2005, 50, 301-380.
- [58]. Eseldin Keleb, Rakesh Kumar Sharma, Transdermal Drug Delivery System-Design and Evaluation, International Journal
- [59]. Ankush I, Shembale, Useful Permeation Enhancers for Transdermal Drug Delivery A Review, IJPRD, 2010, 5, 1-6.
- [60]. Brian W, Barry, Dermatological Formulations Percutaneous Absorption, 18, 95-126.
- [61]. Hadgraft J.W, and Somers G.F, Review Article Percutaneous absorption, International Journal of Pharmaceutics, 2005, 305, 2-12
- [62]. Gilbert S, Banker, Christopher T, Rhodes, Modern Pharmaceutics, 2nd Ed, Revised and Expanded, 40, 263-298
- [63]. Mohamed Aqil, Yasmin Sultana and Asgar Ali, Matrix Type Transdermal Drug Delivery Systems of Metoprolol Tartrate, In vitro Characterization, Acta Pharm, 2003, 53, 119-125.
- [64]. Basubramanian V, Iyer and Ravindra C, Vasavada, Evaluation of Lanolin alcohol films and Kinetics of Triamcinolone Acetonide Release, Journal of Pharmaceutical Sciences, 1979, 68(6), 119-125.
- [65]. Chowdary K.P.R and Naidu R.A.S, Preparation and Evaluation of Cellulose Acetate Films as Rate Controlling Membranes for Transdermal use, Indian Drugs, 1991, 29 (7), 312-315.

- [66]. Mamatha T, Venkateswara Rao J, Mukkanti K, Development of Matrix Type Transdermal Patches of Lercanidipine Hydrochloride, Physicochemical and in-vitro Characterization, DARU, 2010, 18 (1), 9 -16.
- [67]. Sridevi S, Chary M.G, Krishna D.R, Prakash V, Diwan, Pharmacodynamic Evaluation of Transdermal Drug Delivery System of Glibenclamide in Rats, Indian Journal of Pharmacology, 2000, 32, 309-312.
- [68]. Sharma Teja, Rawal Gaurav, Transdermal Therapeutic Systems, An overview, International Journal of Pharmaceutical & Biological Archives, 2011, 2(6),1581-158
- [69]. Sharma Teja, Rawal Gaurav, Transdermal Therapeutic Systems, An overview, International Journal of Pharmaceutical & Biological Archives, 2011, 2(6),1581-1587.
- [70]. Shalu Rani, Kamal Saroha, Navneet Syan, Transdermal Patches a successful tool in Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5),17-29
- [71]. Parthasarathy G, Bhaskar reddy K and Prasanth V.V, Formulation and Characterization of Transdermal Patches of Naproxen with various polymers, Internati
- [72]. Shalu Rani, Kamal Saroha, Navneet Syan, Pooja Mathur, Transdermal Patches A Successful Tool In Transdermal Drug Delivery System: An overview, Der Pharmacia Sinica, 2011, 2 (5), 17-29.
- [73]. Kamal Saroha, Bhavna Yadav, Benika Sharma, Transdermal Patch, A Discrete Dosage Form, International Journal of Current Pharma Research, 2011,3(3), 98-108.