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# Transdermal drug delivery system: A tool for NDDS

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## Abstract

Transdermal drug delivery system (TDDS) specializes to explore new methods that can efficiently and painlessly transmit better molecules in therapeutic quantity to overcome the difficulties allied with oral route, namely poor bioavailability due to first pass metabolism and receptiveness to produce rapid blood level. Transdermal drug delivery gets improved the therapeutic effectiveness and security of drugs by more site-specific way but spatial and temporal placement within body is necessary to reduce both the size and number of doses essential to achieve the objective of systemic medication through topical application to the intact skin surface. Transdermal patches deliver the drugs for systemic effects at a predetermined and controlled rate. Through a diffusion process, the drug enters the bloodstream directly through the skin. The success of all the TDDS depends on the skill of the drug to permeate skin in sufficient quantities to achieve its desired therapeutic effect.

This review discusses the details mechanism of TDDS including its basic components as well as the permeable enhancers. It also provides the limitations and benefits of the Transdermal Drug Delivery System. The recent innovations, nanocarriers and Future prospects of TDDS is also discussed in this review.

**Keywords:** TDDS; Topical drug delivery; Transdermal Patches; Microneedle

## 1. Introduction

There are numerous ways to provide medications these days, each with their own unique delivery mechanism: mucosal, intravenous, transdermal, lung inhalation, and oral[1]. Self-contained, discrete dosage is the definition of transdermal medication administration. Many medications are taken orally, but it has been noted that they are not as effective as intended. To improve this situation, TDDS was developed[2]. To optimize therapeutic effectiveness and minimize negative effects, DDS focuses on formulation and administration procedures that effectively transport medicines[3]. When applied to intact skin, a variety of forms allow the medicine to be delivered to the systemic circulation at a controlled rate through the skin. By guaranteeing longer therapy periods while maintaining controlled drug levels[4]. TDD techniques show great promise in treating chronic diseases. They accomplish this by attempting to achieve controlled molecule permeation across several skin layers[5].

Recent work has demonstrated that delivering drugs to the bloodstream through the skin can be beneficial. The list of medicinal substances that can be injected via the skin and enter the systemic circulation is growing[6]. To topically apply medication to the intact skin surface with the goal of systemic administration[7]. The inability of transdermal drug delivery systems to distribute medications through the skin within the intended therapeutic range has been one of their main shortcomings. Numerous investigations have been conducted on novel drug delivery techniques utilizing cutting-edge micro- and nanotechnologies to get around this restriction[8]. Moreover, TDD is facilitated by both active and

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passive techniques[9]. This transdermal delivery technique involves the preparation of medicated adhesive patches that, when applied to the skin, distribute a therapeutically effective dosage of medication throughout the skin[10]. Nonoral methods may be utilized to eliminate the negative effects connected with the oral administration of NSAID[11]. A patch is one of the transdermal drug delivery systems, which can easily penetrate the drug through skin[12].

The concentration of a drug at the site of action, which depends on the dose form and the degree of absorption of the drug at the site of action, determines the pharmacological response, or the intended therapeutic effect as well as the undesirable side effect[13,14]. Transdermal vaccination delivery may be a more appealing option than traditional subcutaneous or intramuscular injection. since it may be administered at home and because skin has many immune cells[15]. Using a syringe or pumps to gain vascular access is not necessary when using patches applied topically[16]. Transdermal patches have a unique barrier that regulates how quickly the liquid medication within the reservoir of the patch can seep past the skin and into the bloodstream[17].

## 2. Advantages: [5,18,19,20,21]

- Decreases frequency of dose.
- Improves drug bioavailability by lowering drug concentration.
- Escapes the liver's first-pass metabolism.
- Lowers medication plasma levels, which lessens adverse effects.
- Non-invasive, therefore parenteral therapy is not necessary.
- Improves adherence because of prolonged treatment with a single application
- They can stay away from issues with gastrointestinal drug absorption brought on by changes in enzyme activity, gastrointestinal pH, and drug interactions with food, beverages, and other oral medications.
- They can take the place of giving medication orally when it is not the best option, such as in cases of diarrhea and vomiting.
- To prevent the initial pass effect, such as when using transdermal nitroglycerin. When taken orally, It is quickly metabolized by the liner.
- The ability to load hydrophilic, amphiphilic, and lipophilic molecules due to its chemical flexibility.
- Offer appropriate conditions for self-management.
- Regulates the homogeneity of the plasma level.

## 3. Disadvantages [5,18,22]

- Potential skin restricted to strong medications administered trans dermally.
- Some individuals experience irritation at the application location.
- The system's perhaps uneconomical character.
- Drug binding to the skin may result in dosage dumping.
- More appropriate for long-term than for short-term circumstances.
- The medication's effectiveness may be impacted by cutaneous metabolism.
- Ionic medications are not appropriate for transdermal treatment.
- Only appropriate for medications whose molecular weight is less than 500 Daltons.
- Depending on the type of patch and the surroundings, adhesiveness may change.

## 4. Limitations [16,23,24,25]

- Ionic medicines cannot be delivered using TDDS.
- Blood or plasma TDDS levels cannot be raised to high medication levels.
- It is unable to develop large-molecule medicines.
- Drug delivery by TDDS is not pulsatile.
- If medicine or formulation irritates the skin, TDDS cannot form.
- Unsuitable for medications with a large molecular weight.
- To guarantee easy diffusion throughout the SC, a molecular weight of less than 500 Daltan is necessary.
- Sufficient lipid and aqueous solubility; for systemic distribution, the permeant needs to have a log P between 1-3 order to pass through the SC and its underlying watery layers.

## 5. Anatomy and Physiology of Skin

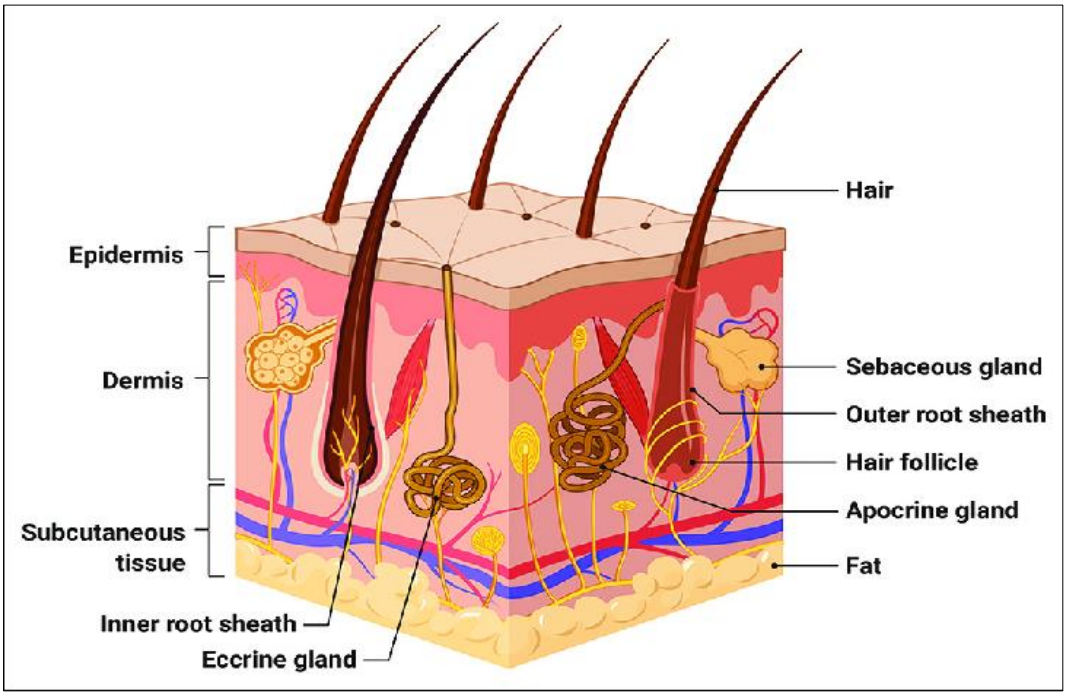


**Figure 1** Structure of Human skin [26]

### 5.1. Epidermis

The largest organ in the body, the skin makes up roughly 6 pounds of our total weight on average. The main roles of the skin are to keep the body hydrated, or to retain water within the body, and to keep outside substances out of the body [27]. Trans appendageal absorption of drugs from the skin is the second route [28]. The stratum corneum, the skin's outermost layer, acts as a physical barrier to absorb substances before they reach the skin. Twenty to thirty layers of dead, flat keratinocytes make up the stratum corneum. These layers are regularly removed, and new cells from deeper layers take their place[29]. Protein (75–85%), mostly keratin, and lipids (5–15%), comprising phospholipids, glycosphingolipids, cholesterol sulfate, and neutral lipid, make up the stratum corneum [30]. Keratin in the corneocytes is linked to water in the stratum corneum [31].

*5.1.1. Function:[25]*

- Being composed of dead cells, it shields the deeper layers from harm and pathogens.
- It functions as a barrier to the flow of substances both inner and outside.
- The skin's outermost layer, the epidermis, contributes to skin tone and acts as a waterproof barrier.
- Beneath the epidermis is the dermis, which is home to sweat glands, blood vessels, lymphatic vessels, hair follicles, and connective tissue.

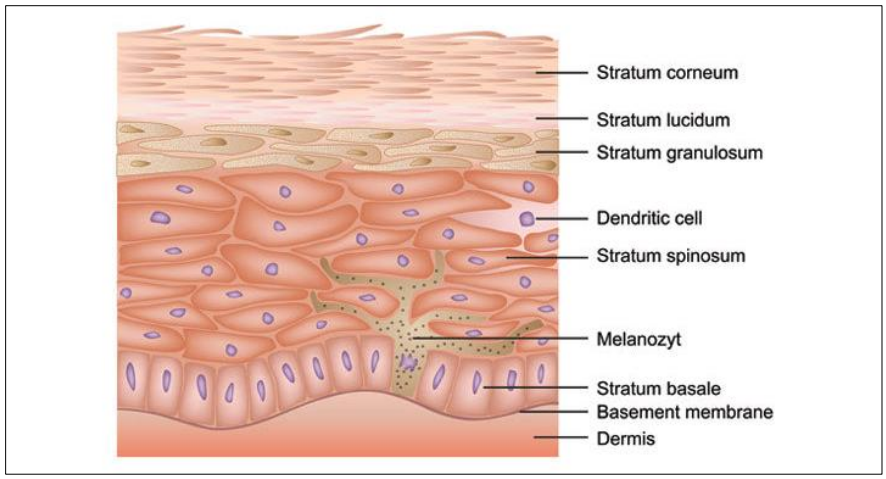


**Figure 2** Structure of Epidermis [5]

### 5.2. Dermis

The dermis is a layer that is 3 to 5 mm thick and is made up of a connective tissue matrix that includes nerves, lymph vessels, and blood vessels. The cutaneous blood supply plays a critical role in regulating body temperature [32]. The cutaneous blood supply is essential for controlling body temperature, supplying the skin with nutrition and oxygen, and removing waste and pollutants. Many molecules can pass through the skin barrier more easily when capillaries are present within 0.2 mm of the skin's surface [33]. The constant flow of blood plays a crucial role in controlling body temperature [34].

#### *5.2.1. Function*

- To uphold and safeguard the epidermis and its deeper layers [35].
- Help sense and help with thermoregulation [36].

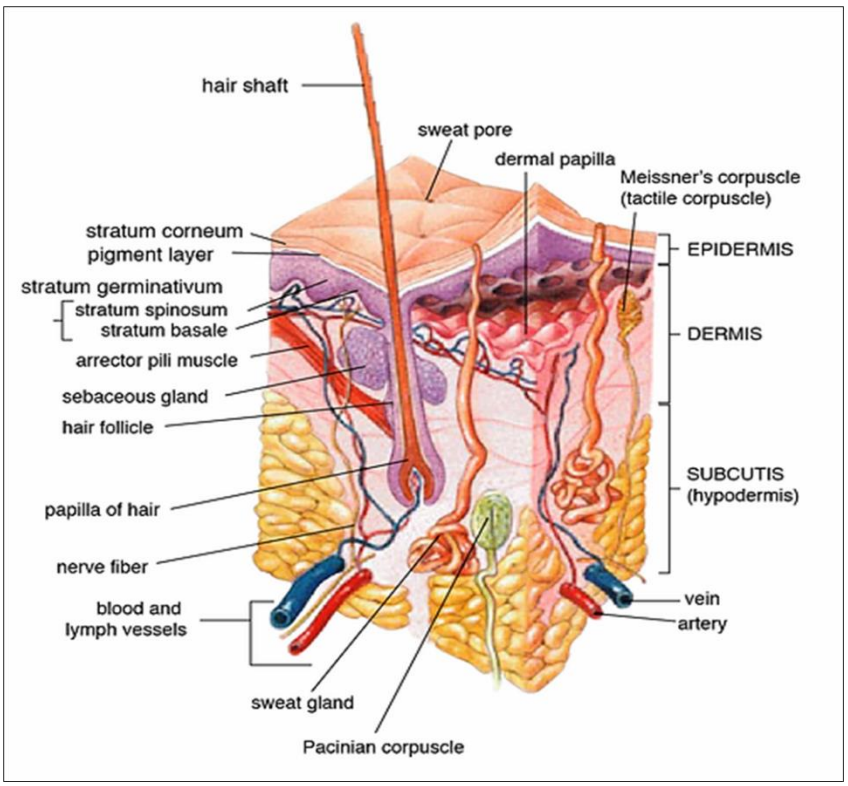


**Figure 3** Structure of Dermis [8]

### 5.3. Hypodermis

The skin on the bottom of your body is called the hypodermis. It serves a variety of vital purposes, including energy storage, bridging the gap between your skin's dermis and your muscles and bones, insulating your body, and shielding it from injury [37,38]. In transdermal drug delivery, the drug must pass through all three of these layers to enter the systemic circulation; in topical drug delivery, just the stratum corneum must pass through for the medication to remain in the skin layers where it is intended [7]. This layer controls temperature and aids in providing mechanical protection for the nutrients [39].

*5.3.1. Function*

- The subcutaneous layer serves as a layer of insulation to safeguard your internal organs.
- Aids in temperature regulation, fat storage, and insulation [40].

## 6. Mechanism of Transdermal Drug Delivery System [41,42,43]

The process involves drug diffusion through the skin's layers, which is regulated by rate-limiting membranes and facilitated by penetration enhancers. Factors including medication characteristics, age, and state of the skin are important in determining how successful transdermal distribution is First, the bio adhesive polymer undergoes wetting or swelling, allowing it to form a tight bond with the mucosal membrane. Then, the polymer chains penetrate the tissue or mucosal membrane surface, enhancing the adhesive interaction and prolonging drug retention.

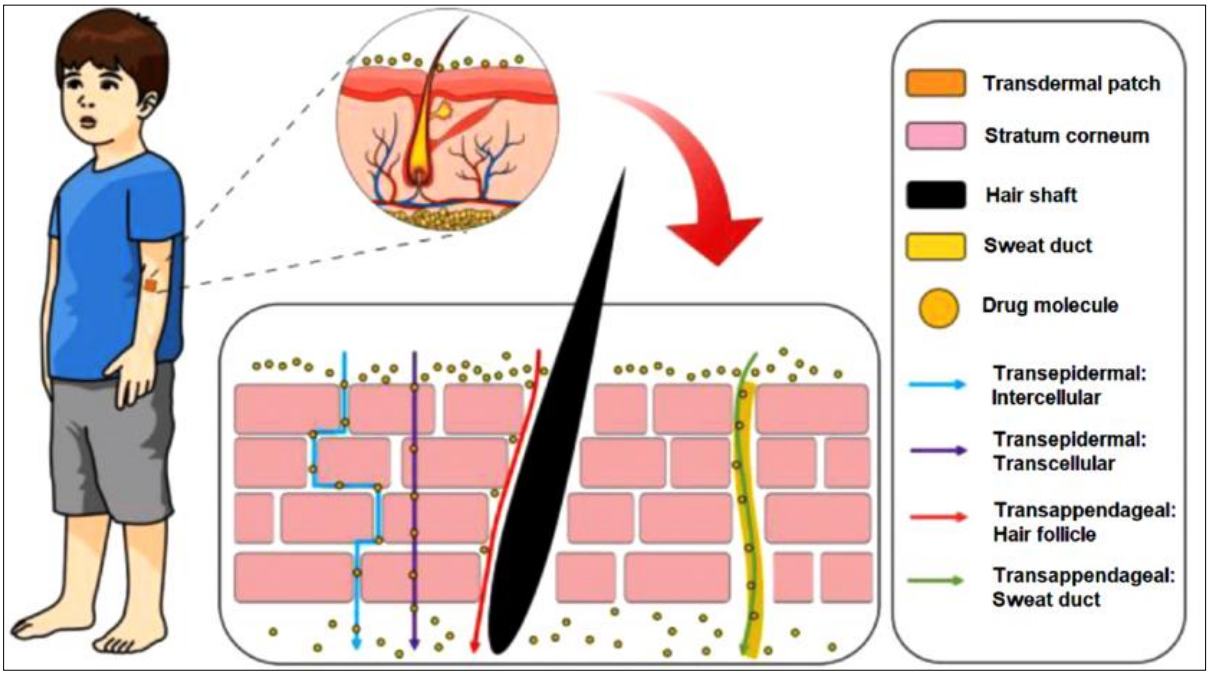


**Figure 4** Mechanism of TDDS[41]

## 7. Basic Component of TDDS

### 7.1. Polymer Matrix/Drug Reservoir

The core of TDDS is polymers, which regulate the drug's release from the apparatus. Drugs can be dispersed in liquid or solid-state synthetic polymer bases to form polymer matrix [44]. The polymer's characteristics, such as its molecular weight, glass transition temperature, melting point, and chemical activity, should allow the medicine to diffuse through it and interact with other system components with ease [45]. The transdermal drug delivery method is built on polymers. Transdermal delivery systems are made of multilayered polymeric laminates in which a drug reservoir or drug polymer matrix is switched between two polymeric layers: an inner polymeric layer that acts as an adhesive or rate-controlled membrane, and an outer polymeric layer that is impervious to drug loss through the backing surface [46]. Polymers are the backbone of a transdermal drug delivery system. Systems for transdermal delivery are fabricated as multi layered polymeric laminates in which a drug reservoir or a drug polymer matrix is sandwiched between two polymeric layers,

an outer impervious backing layer that prevents the loss of drug through the backing surface and an inner polymeric layer that functions as an adhesive, or rate-controlled membrane [47].

*7.1.1. Ideal Properties of Polymer Matrix [46,48]*

- The polymer needs to exhibit stability.
- The polymer ought to be non-toxic.
- It should be simple to make the polymer.
- The polymer must be reasonably priced.
- Both the polymer and its degradation product ought to be non-toxic or non-aggressive towards the host.

### 7.2. Drug Substance

Medicine must be carefully chosen to build a transdermal drug delivery system that works. Some of the desired characteristics of a medication for transdermal distribution are listed below the transdermal patch's drug exhibits proper chemistry and activity. Transdermal patches medication passes through a thorough first pass metabolism before beginning to have a therapeutic effect on the body [46].

### 7.3. Permeable Enhancer

To create a transdermal drug delivery system that functions, the medication must be properly selected. Below is a list of some of the qualities that a drug intended for transdermal delivery should have combination of polymers [46]. Compounded HMPSAs include ethylene vinyl acetate co-polymers, low density polypropylene, paraffin waxes, styrene-butadiene copolymers, and ethylene-ethacrylate copolymers. Uncompounded HMPSA includes materials like polyesters, polyamides, and polyurethanes [49]. The medicine in the transdermal patch has the right activity and chemistry. Before starting to have a therapeutic effect on the body, the drug in transdermal patches goes through a rigorous first pass metabolism. For instance, nitroglycerine, fentanyl, and topiramate [50].

*7.3.1. Ideal Properties of Penetration Enhancers[46]*

- 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.

### 7.4. Pressure Sensitive Adhesive

One kind of material that's employed to keep the transdermal system and skin surface in close contact is called pressure sensitive adhesive, or PSA. It should be adhered using finger pressure alone and given a powerful gripping force. It should be simple to remove and leave no trace, like polyacrylates, polyacrylamides, and polyisobutylene [51]. Choosing an adhesive involves numerous factors, two of which are the drug's content and the patch's design. Adjacent for physical stability should not alter medication release and should be biocompatible [50]. It should be simple to remove, doesn't irritate or sensitize skin, and has good skin contact and laminating layer bonding [52].

### 7.5. Backing Laminant

Good tensile strength and flexibility are requirements for backing materials. Materials such as polyesters, elastomers, and polyolefins in clear pigmented or metallized forms are frequently utilized. Better adherence and greater conformity to skin movement are provided by elastomeric materials like low-density polyethylene than by less flexible polymers like polyester. To encourage improved skin permeability and increased skin hydration, backing materials should also have low water vapour transmission rates [53,54]. The backing material in systems that hold drugs in liquid or gel must be heat-sealable to enable fluid-tight packing of the drug reservoir using the form-fill-seal method. The backing with the highest rate of moisture vapour transmission, good oxygen transmission, lowest modulus or great flexibility will be the most comfortable [44,47]. They should have a low moisture vapour transmission rate and ideal levels of elasticity, flexibility, and tensile strength. Excipients and chemical resistance should be suitable when developing the backing layer because extended contact between the backing layer and the layer enhances penetration through the layer [51].

### 7.6. Release Liner

The release liner stops drug loss and contamination while the product is being stored. Even though the liner comes into direct touch with the delivery system, it nevertheless meets all the standards for chemical inertness and water and drug penetration [45]. Drug loss from migration into the adhesive layer and contamination is avoided during storage thanks to linear release [46].

### 7.7. Other Excipient

A range of solvents, including dichloromethane, acetone, methanol, isopropananol, and chloroform, are employed in the preparation of drug reservoirs. To provide transdermal patch flexibility, additional plasticizers like propylene glycol and dibutylphthalate are added [46]. Furthermore, plasticizers such polyethylene glycol, propylene glycol, dibutylphthalate, and triethyl citrate are added to give the transdermal patch its fluidity [44,55]. The liner should be chemically inert, permeability to the medicine, penetration enhancers, and water-resistant because it will be in close contact with the delivery system [56].

## 8. Transdermal Patch

In virtually every transdermal patch design, the medication is kept in a reservoir with an adhesive side that comes into touch with the skin and is contained on one side with an impermeable backing. Certain designs utilize a medication that has been dissolved in a gel-based or liquid-based reservoir, which can facilitate the use of liquid chemical enhancers like ethanol and simplify formulations. An adhesive layer, a semi-permeable membrane that could act as a rate-limiting barrier, a drug reservoir, and an impermeable backing membrane make up the four layers that are typical of these designs. In other designs, the medication is included into a solid polymer matrix, which facilitates production [57]. Matrix systems can consist of two layers if the medicine is mixed into the adhesive directly, or three layers if the semi-permeable membrane is removed [49,58]. In a transdermal passive therapeutic system, a drug is injected under the skin at a consistent pace over a predetermined period with an effective systemic concentration. These investigations have shown that more adhesives are removed along with the patch when it is removed more slowly [59].

## 9. Types of Transdermal Patch

**Single layer drug in adhesive: In this kind**, the medicine is included in the sticky layer. In addition to holding several layers together, the adhesive layer oversees delivering the medication to the skin[61]. The ability of an adhesive layer to stick different layers together is in addition to its role in delivering the medicine to the skin[58].

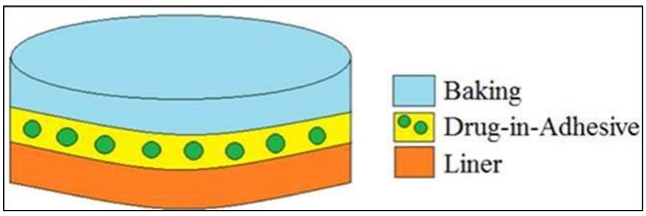


**Figure 5** Single layer a drug in adhesive [62]

Multi-layer Drug in Adhesive Multiple-layered drug-containing adhesive patches are comparable to monolayer systems in that both layers aid in the drug's release. However, the extra layer of pharmaceutical adhesive, which is often separated by a membrane, is what differentiates them[5]. This medication-containing polymer disk is installed in a compartment made of a drug-impermeable backing layer, fixed to an occlusive base plate, rather than covering the drug reservoir's face with adhesive. It is dispersed around the perimeter to create an adhesive rim strip[61,63]. In multilayer systems, it has a backing laminate and a transits protective layer. Multi-layer patches are used to administer hormone therapy, smoking treatments, and pain relief for a maximum of seven days[61,64]. By multilayer system it is possible to achieve the mechanical interlocking adhesion by increasing the volume of swellable tips.

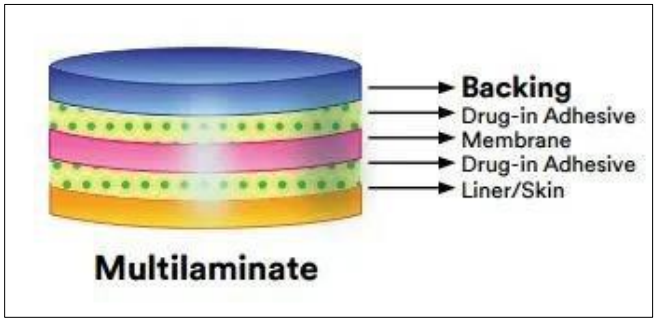


**Figure 6** Multilayer Drug in Adhesive[65]

**Drug Reservoir in Adhesive Adhesive layer**, release liner, baking layer, and semi-permeable membrane are placed in order of appearance in the reservoir system, together with a liquid compartment holding drug solution or suspension[46]. The polymeric membrane, which regulates drug release gradually, is composed of components such as ethylene vinyl acetate copolymer and hypoallergenic sticky polymer. The drug layer in this approach creates a liquid compartment that is divided from the supporting layer and contains a drug solution or suspension. Interestingly, the release rate exhibits a zero-order pattern in this configuration[26]. To create the drug reservoir for this kind of patch, the medication is combined with an adhesive polymer. Spreading an impermeable backing layer using a melting or solvent casting technique came next. An unmediated sticky polymer film covers the reservoir's top for protection. It can also be divided into drug-in-adhesive single-layer and multi-layer categories. Many different types of medications are thought to work well with system[66]. There is a different medication layer in this transdermal system. The backing layer separates the drug layer, which is a liquid compartment that adheres to a drug solution or suspension. There is zero order release rate in this reservoir system[65]. It is possible to apply hypoallergenic adhesive polymer as a drug-compatible outer surface polymeric membrane[67].

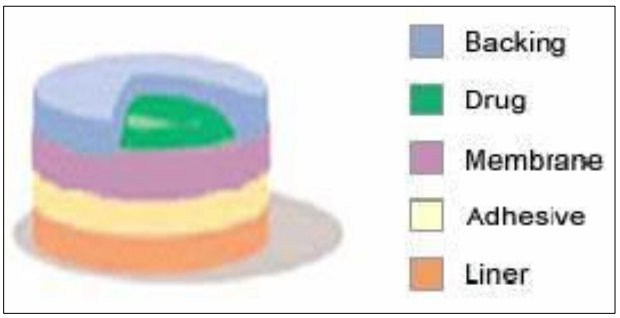


**Figure 7** Drug Reservoir in Adhesive [68]

Drug Matrix in Adhesive This kind of medication has a uniform distribution throughout a hydrophilic or lipophilic polymer matrix. The drug-containing polymer disk is affixed to an occlusive base plate within a compartment made of a backing layer impervious to drugs. The glue is dispersed around the perimeter to create an adhesive rim strip rather than being applied on the face of the drug reservoir[69]. Within a compartment composed of an impermeable drug backing sheet, this drug in the form of a polymer disk is bonded to an occlusive base plate. After stretching it along the perimeter to form an adhesive film strip, the adhesive is applied to the drug reservoir's layer[66]. The medication may be found as a gel, liquid, suspension, or solid polymer matrix within the drug reservoir compartment. It is feasible to employ a polymeric membrane whose outer surface is hypoallergenic and drug compatible[70].

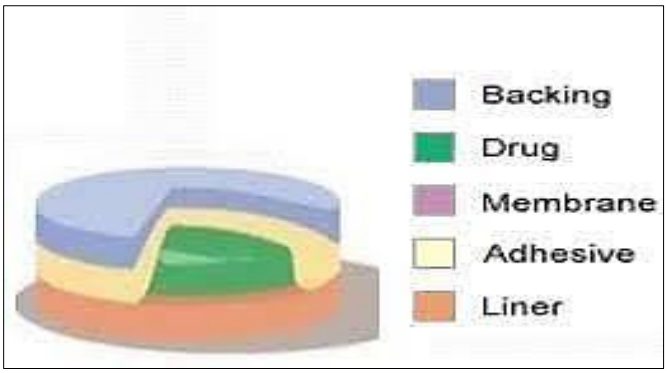


**Figure 8** Drug Matrix in Adhesive[62]

**Vapour Patch In this kind of patch**, the layer of adhesive serves the dual purpose of holding the several layers together and enabling the vapor to escape. For up to six hours, these vapour patches, a relatively new product on the market release essential oils[71]. Products such as Nicoderm, which are transdermal patches that vaporize nicotine and incorporate essential oils to help people stop smoking, serve as an example of these patches. Furthermore, a variety of additional vapor patch varieties are on the market, with uses including improving sleep quality and mitigating the effects of cigarette smoking[5]. Numerous different kinds of vapour patches that are intended to lessen the problems associated with cigarette smoking and enhance sleep quality are also offered on the market[66]. Recently introduced vapor patches provide up to six hours of important ailment release. The main purpose of the vapor patches is to relieve

congestion and release essential oils[60]. Recently introduced to the market, vapor patches are frequently used to release essential oils to relieve congestion[72].

## 10. Evaluation Parameters

### 10.1. Thickness[74]

Film Thickness can be measured by using micrometer, dial gauge, screw gauge, or traveling microscope at various locations along the film.

### 10.2. Determination of drug content in the patches[73]

By using UV spectroscopy drug content of patches can be determined. Phosphate buffer of pH 7.4 is used as a solvent. In this method the film is cut to a small piece and dissolve in appropriate solvent, and then the solution is filtered after being agitated with a mechanical stirrer to create a uniform mixture. After extracting the 1 ml filtrate and diluting it to 100 ml, 1 ml of solution can pipette and diluting it to 10 ml with pH 7.4.

### 10.3. Solubility Study[76]

Solubility study is an important key factor since it is directly correlated with its ability to be absorbed into the bloodstream without the usual formulation. The drug's solubility is investigated in a variety of different solvents, including ethanol, water, dimethyl formamide, DMSO, benzyl alcohol, and phenol.

### 10.4. Water vapour permeability (WVP) evaluation[66]

The foam dressing method is used to measure the water vapour permeability of an air forced oven that is replaced with a natural air circulation oven. This formula is used to find the WVP.

$$\mathbf{WVP} = \frac{\mathrm{W}}{\mathrm{A}}$$

Where W is the quantity of vapour permeated through the patch stated in gm/24 hours, A is the surface area of the exposure samples expressed in $m^2$, and WVP is represented in $gm/m^2$ per 24 hours.

### 10.5. Partition coefficient[64]

The partition coefficient is used to determine the concentration of drug between two immiscible phases. This method is also known as distribution law in which solubility of drug is determined between two immiscible phases, one phase is organic and the other is aqueous.

Formula for determining the partition coefficient is,

$$\mathrm{K} = \frac{\text{concentration. of organic phase}}{\text{concentration. of aqueous phase}}$$

### 10.6. Shear Adhesion Test[75]

It is employed to gauge the adhesive polymer's cohesive strength. To cause adhesive film to pull in a direction parallel to the plate, it is laid over a stainless-steel surface and a certain amount is suspended from the tape. The amount of time required to pull the tape off the plate is used to determine the shear adhesion strength. The shear strength increases with increasing removal time.

### 10.7. Peel Adhesion Properties[75]

The force needed to separate the adhesive film from the substrate is known as the peel adhesion. This test measures the force needed to pull a single coated tape. At 180°C, the coat must be applied to the substrate.

### 10.8. *In-vitro* Drug Release Studies[68]

One technique for evaluating the drug release of patches is the paddle over disc method. For this the dry film is precisely sliced to a precise size and shape. Next, the cut patch piece is adhered to a glass plate using adhesive. The 500 ml dissolving medium which is added to the cylindrical vessel is then filled with plates. The temperature is kept at 30° +/-

5°C, and the paddle is positioned 2.5 cm from the bottom glass plate. RPM is set at 50. The samples are taken at appropriate intervals of up to 24 hours, with fresh medium replaced between each sample.

### 10.9. Percentage Moisture content[75]

Transdermal film is weight and stored in a desiccator with calcium chloride at room temperature for 24 hours. The films are weighed again at regular intervals until they have consistent weight. The percentage moisture content is computed using the formula.

$$\text{Percentage moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

### 10.10. Organoleptic Evaluations[77]

Physical properties of film such as color, odor, and taste can be evaluated to check the quality of drug.

### 10.11. Skin temperature[78]

Raising skin temperature causes an increase in skin permeability. Increased skin temperature may also cause dilatation of blood vessels in contact with the skin, resulting in increased percutaneous absorption.

## 11. Recent Innovations in Transdermal Drug Delivery System:

### 11.1. Advance Development in TDDS[79]

To achieve improved transdermal delivery and therapeutic efficacy, drugs must have a low molecular weight [less than 1 kDa], affinity for both lipophilic and hydrophilic phases, a short half-life, and a low risk of causing skin irritation. Drug penetration through the skin is influenced by a variety of factors[80].

Drug-in-adhesive technology has emerged as the dominant approach for passive transdermal distribution; adhesives and excipients are the focus of formulation development. Adhesive research focuses on tailoring the adhesive to improve skin adhesion over time, drug stability and solubility, lag time reduction, and delivery rate increase. Customizing the adhesive is necessary because there is no one-size-fits-all glue that can accept all medication and formulation chemistries. Chemistry enables the transdermal formulator to maximize the performance of the transdermal patch polymer. TDDS is a viable and practical application for the next generation of drug delivery systems. The database of the Spanish Agency for Medicines and Medical Devices was used in December 2022 to identify marketed transdermal medication delivery solutions[81].

### 11.2. Nanotechnology gaining hold

This method combines the advantages of needles and transdermal patches[82]. The gadgets are dime-sized polymer chunks with hundreds of hollow microneedles (100-1000 micrometers long). These little needles penetrate the upper layers of skin, allowing the medicine to pass through with ease[27].

### 11.3. Nanocarriers in Controlled Drug Delivery

#### *11.3.1. Liposome*

These are the particles formed when lipid bilayers and amphiphilic phospholipids mix to form an aqueous compartment[82]. The hydrophobic effect creates a closed bilayered structure, facilitating the arrangement of amphiphilic molecules and reducing unfavorable interactions between hydrophobic chains and the surrounding aqueous environment. Depending on the polar head group, phospholipids can be either phosphatidylcholine or phosphatidylserine. Phosphatidylcholine is often employed in liposome synthesis[83]. Liposomes are artificially created lipid bilayer vesicles that are commonly utilized as vehicles in medicines and cosmetics for regulated drug delivery to specific parts of the skin or its layers[84].

#### *11.3.2. Polymerosomes*

Liquid medications are kept in small polymersomes composed of synthetic materials. These are often made from copolymers and polymer-lipid composites because they have superior membrane characteristics, encapsulation

efficacy, and colloidal stability. Polymersomes have been found to be more stable and safer for the body than liposomes. They are suitable for encapsulating both hydrophobic and hydrophilic medicines[36].

*11.3.3. Dentrimers*

The term "dentrimer", which means "tree", comes from Greek and refers to something resembling a tree's branches. Dendrimers have a three-dimensional structure shaped like a sphere and are symmetrical around the core. They are constructed using monomers, which might be natural or synthetic [65]. They are composed of a control core surrounded by layers of polymers[85].

*11.3.4. Exosomes*

Cells create exosomes, which are nanosized membrane-bound vesicles ranging in size from 30 to 100 nm. They facilitate the movement of both foreign and endogenous chemicals between cells. Exosomes can transport a variety of medicinal substances, including small proteins, mRNA, and nucleic acids. These molecules can then be directed to certain cell or tissue types for targeted medication administration. They have been widely used and rapidly developed in recent years due to their significant potential for internalization with cells. Exosomes, both natural and manufactured, are used to transport peptides and genes[65].

*11.3.5. Transformers*

Depending on their composition, some liposomes may have a flexible shape and flow through the SC while others aggregate in the SC's channel-like regions. The driving mechanism is simply osmotic pressure, and these liposomes are known as transfersomes or transformable liposomes[86].

### 11.4. Currently Approved Transdermal Delivered Drugs[65]

The TDD market has a significant impact on drug delivery, particularly in the areas of pain management, hormonal applications, central nervous system disorders, cardiovascular diseases, and other applications such as smoking cessation. The global transdermal medication delivery industry is expected to be rather significant. The prevalence of chronic diseases and technological advancements in transdermal medication delivery systems are propelling this market ahead. In 1979, the United States approved the first transdermal patch for systemic administration. A three-day patch that supplied scopolamine to cure motion sickness. The most current FDA-approved patch for severe pain is buprenorphine, which is used to treat chronic pain that does not respond to other drugs. There are also various over the counter (OTC) products available, such as nicotine, capsaicin, and menthol patches. In 2018, the Japanese market system approved the first antihistamine medication transdermal patch, Emedastine, Difumarate, recommended to treat allergic rhinitis. It has a dose-dependent anti-histaminic impact and a long-lasting effect that can persist up to 24 hours after injection.

### 11.5. Future Prospects for Transdermal Drug Delivery Systems[65]

In recent years, there has been a strong emphasis on creating sophisticated transdermal delivery systems that use non-invasive or minimally invasive technology to increase drug delivery through the skin. These technologies include iontophoresis, microneedles, electroporation, and sonophore. Their goal is to improve medicine delivery in areas where low penetration flux and potency have traditionally been a problem. However, the development of active patches based on these technologies has encountered challenges in terms of economic success, technical problems, and customer acceptance. One of the most recent innovations in drug delivery systems is the use of micro-needles, which has received a lot of attention. They show potential in delivering antigens to the skin and eliciting antibody responses similar to traditional intramuscular injections. Microneedles have also been studied for the long-term treatment of opiate and alcohol dependence using naltrexone, an opioid antagonist. In addition, Zosano Pharm's micro-needle patch coated with parathyroid hormone has shown efficacy in Phase II clinical studies for osteoporosis. To summarize, the pharmaceutical industry is looking into non- and minimally invasive technologies such as iontophoresis, microneedles, electroporation, and iontophoresis to improve drug delivery via the skin. However, despite initial achievements and promising improvements, several difficulties have prevented the general commercialization of active patches that employ these technologies.

Nonetheless, while transdermal delivery can be viewed as an accessible, non-invasive method of drug delivery for term babies and aged children consuming lesser boluses than adults, expression issues persist for unseasonable babies with an undeveloped skin barrier[65]. The current scenario has evolved as the safest and most skin-acceptable mode of drug delivery to the system (circulation, anti-oral route)[87].

## 12. Conclusion

Transdermal medication administration is becoming the most widely used route due to recent technological developments and the medicine's ability to reach the site of action without rupturing the skin membrane. This article is a great resource for researchers studying transdermal drug delivery systems (TDDS) because it contains a wealth of information about the formulation and evaluation aspects of these systems. The information above shows that TDDS has a lot of potential because it can be utilized to create effective drug delivery systems from both hydrophilic and hydrophobic active ingredients. A deeper comprehension of the many biological interactions and polymer mechanisms is needed to improve this drug delivery technology.

TDDS represents a feasible and useful for the upcoming generation of drug delivery technologies. This field's comprehension of skin anatomy and physiology is more thorough. We must learn more about biological interactions to optimize this system. There is a use for TDDS, the next generation of drug delivery.

## Compliance with ethical standards

*Disclosure of conflict of interest*

No conflict of interest to be disclosed.

## References

[1] Tabade M, Zendekar P, Sanap G. Review on Transdermal Drug Delivery System. world Journal of Pharmaceutical and Medical Research. 2024;10(1):225-232.

[2] Chaudhary N, Singh P. A. A Review Article on Transdermal drug delivery System. Indian Journal of Pharmacy and Pharmacology. 2021;8(1):5-9.

[3] Joshi N, Machekposhti S, Naraya R. Evaluation of Transdermal Drug delivery devices & Novel microneedle Technologies. A Historical Perspective & Review. 2023;(30):1-10.

[4] Hafeez A, Jain U, Rana L. Recent Advances in Transdermal Drug delivery System. Journal of scientific Innovative Research 2013;2(3):695-709.

[5] Deulker AD, kubde J, Hatwar P, Bakal R. A review on Transdermal Drug Delivery system GSC. Advance Research and Reviews. 2024;18(02):347-36.

[6] Peddy YK, Reddy MD, Kumar AM. Transdermal Drug Delivery System A Review. Indian Journal of Research in Pharmacy & Biotechnology. 2014;2(2):1094-1104.

[7] Tandale M. A, Hingane LD. Formulation & evaluation Aspects of TDDS. International Journal of creative Research Thought.2021;9(12).

[8] Bedre A, Bhoge D, Ige P. Review on Transdermal Drug delivery System. Focus on Innovative Transdermal Dosage Forms. Journal of Pharmaceutics & Drug development. 2023;10(2).

[9] Schafer N, Balewierz R, Biernat P, Lipok J. Natural ingredient of TDDS as Permeation Enhancers. Molecular pharmaceutics.2024;20:3278-3297.

[10] Kadam A, Ratnaparkhi P. M, Chaudhary P. S, Transdermal Drug Delivery system An overview. International Journal of Research & development in Pharmacy and life science. 2014;3(4):1042-1053.

[11] Rastogi VP, Transdermal Patches A Synergistic Approach of Drug Delivery For NSAIDs. International Journal of Pharmaceutical Science and research 2012;3(9):2897-2909.

[12] Mahdiyyah A. A, Diyah W. N, Hendradi E, Transdermal patches A Review of new drug delivery system Approach. International Journal of Medical Reviews & case Report. 2022;6(9);25-31.

[13] Zhan X, Man Z, Wang L, Formulation and evaluation of transdermal drug delivery system of isosorbide dinitrate. Brazilian Journal of Pharmaceutical sciences. 2015;51(2):373-38.

[14] Sharma N, Agrawal G, Rana A. C, Kumar D. A Review on TDDS: A tool for NDDS. International Journal of Drug Development of Research. 2011; 3:70-84.

[15] Zhu W, Wei T, Xu Y, Jin Q, Chao Y, Lu J, Xu J, Zhu J, Yan Y, Chen M, Chen Q, Liu Z. Non-invasive transdermal delivery of biomacromolecules with fluorocarbon modified chitosan for melanoma immunotherapy and viral vaccines,2024, 1-15.

[16] Patel D, Chaudhary A. S, Parmar B, Bhura N. Transdermal Drug Delivery System. The Pharma innovation. 2012;1(4):66-75.

[17] Ghume KV, Golhar RA, Dhoke DM, Parjane KS. Transdermal Drug delivery system: A Review. American Journal of Pharmaceutical Research. 2020;10(2):34-47.

[18] Premjeet S, Bilandi A, Kataria S, Middha A. Transdermal Drug Delivery System Application in present scenario. International Journal of Research in Pharmacy & chemistry. 2011;1(4):1139-1151.

[19] Ghulaxe C, Karpillai M, Pillai S, Kushwah P, Mansare R. Review on Transdermal Drug delivery system. World Journal of Pharmaceutical and Medical Research 2017;3(8):63-71.

[20] Halder S, Chakraborty P, Bagchi A. Recent Advancement in the method of Transdermal Drug Delivery system. Journal of Applied Pharmaceutical Research. 2021;9(2):69-75.

[21] Pagar R. L, Khandbahale V. S. A review on Novel Drug Delivery system. Asian Journal of Pharmacy and Technology. 2019;9(2):135-140.

[22] Chaurasiyal P, Ganju E, Upmanyu N, Ray KS, Jain B. Transferosomes A novel technique for transdermal drug delivery. Journal of Drug Delivery Therapeutics. 2019;9(1):279-285.

[23] D. Prabhakar, J. Sorrekanth, K.N. Jayaveerg. A Review on Transdermal drug delivery System. Journal of Drug delivery and Therapeutics. 2013;3(4):213-221.

[24] Brown B. M, Martin P. G, Janes A. S, Akomeah F. Dermal & Transdermal drug delivery systems. Current and Future prospects. 2006;13(3):1175-188.

[25] Brooks Z, Goswami T, Doll A. Gaswam T. Transdermal Drug Delivery system Analysis of Adhesion Failure, Biochemical Industrial & Human Factors. Engineering Faculty Publication. 2022;4(1):256- 270.

[26] Chu C, Yang C, Tsa S, Hidradenitis Suppurativa:Disease Pathophysiology and Sex Hormones. Chinese Journal of Physiology. 2021;10(3):257-265.

[27] Bhate R, Kapoor R. Transdermal Drug Delivery system Formulation development and Evaluation An Overview. International Research and Advance Research. 2015;6(1):1-10.

[28] Ramadan D, Mecrudden M, Courtenay J. A, Dennelly F. R. Enhancement strategies for transdermal drug delivery System. Current trends & Application. 2022;12(4):758-791.

[29] Chavan S. Y, Shinkar M. D, Jadhav S. S, Pingalk L.P. Boraste S.S, Amrutkor N.S. A simple reach at the Transdermal Drug delivery system. Pharmacophore. 2022;13(3);72-80.

[30] V. Sirisha, Sailaja Ak. Review on Recent Approaches in Transdermal Drug delivery system. Journal of Nursing & patient Health care. 2019;1(3):1-12.

[31] Chatterjee A, Mahanti B. Transdermal Drug Delivery system A Novel Approach to deliver potent Therapeutic Agent. World Journal of Pharmaceutical and Medical Research. 2022;8(5):225-245.

[32] Purushotham K, Vijetha A. K. A Review on Transdermal Drug Delivery system. GSC Biological & Pharmaceutial sciences. 2023;22(2):246-255.

[33] Kamble V.V. Transdermal Drug Delivery System. International Journal of creative Research thoughts. 2021;9(5):7-18.

[34] Sharma R, Nagle A, Patil K. R. A Review on strategically designed drug delivery system W.S.R. To Rasa formulation. World Journal of Pharmaceutical science and Research. 2020;6(11):135-137.

[35] Choudhari R. P, Pahl G. S, Pawar P.S. Niosomes Review Articles. World Journal of Pharmaceutical and Medical Research. 2024;10(6):165-169.

[36] Pasupuleti P, Bandarapalle K, Cherlopalli S, Gundam N, Chilakala A, Chithrala V, Sai G. Transdermal Drug Delivery Systems. Journal of Drug Delivery & Therapeutics. 2023;13(2):101-109.

[37] Nandre PH, Puranik P, Giram P, Ethosome A novel Drug carrier. International journal of pharmaceutical research and Allied Science. 2013;7(3):18-30.

[38] Jayaprakash R, Hameed J, Anupriya. An overview on Transdermal delivery system. Asian journal of Pharmaceutical Research. 2017;10(10):36-40.

[39] Hussein G, Elhaj M. B, Ali S. H. Concept Current Approaches in TDDS. A multifaceted Review Journal in the field of Pharmacy. 2021;12(7):411-418.

[40] Mal N, Bhunia A, Mahanti B. A comprehensive overview of controlled Drug Delivery system. World Journal of Pharmaceutical and Medical Research. 2024;10(6):316-327.

[41] Kumar A, Pullakandam N. S, Prabil L. S, Gopal V. Transdermal Drug Delivery System An overview. International Journal of Pharmaceutical Sciences Review and Research. 2010;3(3):49-54.

[42] Ramadon D, McCrudden M, Courtenay J. A Donnelly FR. Enhancement strategy for transdermal drug delivery systems. Current trends and applications, Drug Delivery and Translational Research. 2022;(10):578-571.

[43] Negi P. K, Tyagi Y, Dr. Rao R. N. A Review on Transdermal Drug Delivery system for Antihypertensive Drug. World Journal of Pharmaceuticals and Life Sciences. 2020;6(6):70-75.

[44] Sachan R, Bajpai M. Transdermal Drug Delivery system. International Journal of Research and development in Pharmacy and life sciences. 2013;3(1):773-790.

[45] Tanwar H, Sachdeva R. TDDS A Review. International Journal of Pharmaceutical sciences and Research. 2016;7(6):2274-2290.

[46] Jain A, Shakya K. A, Prajapati S, Eldesoqui M, Sanjay N, Jain K, Naik R. R, Patil U. An insight into pharmaceutical challenges with ionic liquids, where do stand in transdermal delivery? Frontliner in Bioengineering and Biotechnology. 2024; 9-16.

[47] Tapfumaneyi P, Imran M, Roberts S.M. Recent Advances and future prospective of topical and Transdermal delivery system. Frontliners in Drug Delivery. 2022;1-8.

[48] Shaikh N, Shrivastava R. A review on Transdermal drug delivery Through Patches. IP Indian Journal of clinical and Experimental Dermatology. 2024;10(2):113-121.

[49] Bidkar S, Tandale A, Meher A, Bidkar J, Dama G, Overview of Anti-hypertensive system. International Transdermal Drug Delivery Journal of Drug Delivery Technology. 2023;18(4):1640-1645.

[50] Sirinivas M, Uddin M, Goud M. An overview of Transdermal Drug Delivery System. IJSDR. 2021;6(12):274-283.

[51] Yadav P, Tiwari P, Singh A. Transdermal Patch A Recent Review to Transdermal Drug Delivery System. Journal Of Emerging Technologies and Innovative Research. 2020;7(7):702-719.

[52] Prausnitz M, Langer R. Transdermal Drug Delivery System. Nature Biotech. 2005; 26(11):1261-1268.

[53] Raju G. M, Srinija K. M, Reddy V, Sravyd P. Transferosome A Novel Transdermal Drug Delivery System for the Treatment of Hyperlipidemia. Asian Journal of medical Principles and Clinical Practice 2023;6(2):318-326.

[54] Jhawat C. V, Saini V, Kamboj S, Maggon N. Transdermal Drug Delivery System Approaches & Advancement in Drug Absorption through Skin. International Journal of Pharmaceutical Science Review and Research. 2013;20(1):213-221.

[55] Rajeshwari S, Prashant T, Shrilaxmi N, Gayathri T, A Review on Transdermal Drug Delivery System A Novel Tool for Improving Bioavailability. Innovare Journal of Science. 2021;9(4):1-7.

[56] Cheng C, Tai Z, Ying li M, YJ L, Chen Z, Advance and challenges in the Treatment of skin diseases with the Transdermal Drug Delivery System. Pharmaceuties. 2023;15:1-23.

[57] Shinde P. S, A Review on Transdermal Drug Delivery System. Internal Journal of creative Research Thoughts. 2024;12(1):843-859.

[58] Gunda RK, Kumar JNS, Prasad ABS, Bhargavia B. S, Padmaja KNVL, Praveens. Transdermal Drug Delivery System as Emphasis on Transdermal Patches. Pharmaceutical Drug Regulatory Affairs Journal. 2023;6(1):20-31.

[59] Krishnarajan D, Varadharajan V, Gowtham D. D, Gobi N, Vasudevan P. Recent Approaches of Transdermal Drug Delivery System. Pharmacophore. 2016;7(4):227-244.

[60] Nagdev A. S, Agrawal O, Usman Md R. Transdermal Drug Delivery System An Overview. Research J. Pharm. and Tech. 2022;15(3):1371-1377.

[61] Li Li Z, Fang X, Yu D. Transdermal Drug Delivery system and Their use in obesity Treatment. International Journal of Molecular sciences. 2021; 22:1-23.

[62] Trivedi D, Goyal A, Formulation and evaluation of Transdermal patches containing dexketoprofen trometamel. International Journal of Chemistry and Analysis. 2020;7(2):87-97.

[63] Shinde N, Manikpuriya S, Sanap G. A Review of Transdermal Drug Delivery System, World Journal of Pharmaceutical Research. 2024;13(1):835-857.

[64] Alam A, Machale V. M, Yadav P. R, Patel K. A. Role of Transdermal Drug Delivery system. Asian Journal of Pharmaceutical Research and Development. 2021;9(3):137-143.

[65] Patel V. A, Shah N. B. Transdermal Drug Delivery System A Review. An international Journal of Pharmaceutical Sciences. 2018;9(1):378-390.

[66] Alam F, Machale V, Yadav P. R, Patel K. A. Role of Transdermal Drug Delivery system, Asian Journal of Pharmaceutical research and Development. 2021;9(3):137-143.

[67] Kumar G. H, Transdermal drug delivery system an overview. International Journal of Research in Pharmaceutical Sciences. 2012;3(3):451-457.

[68] Kumar R, Mishra R, Saluja S. M. Transdermal Drug Delivery System. Journal of survey in Fisheries sciences. 2023;10(3):236-240.

[69] Li Ching Ng, Gupta M, Transdermal drug delivery systems in diabetes management A review. Asian Journal of Pharmaceutical Sciences. 2020; 15:13–25.

[70] Shingade A. M, Quazi A, Sabale P. M, Grampurchit N. D, Gadhavemu, Jadhav SL, Gaikwad DD. Review on Recent Trend on Transdermal Drug Delivery system. Journal of Drug delivery and Therapeutics. 2012;2(1):66-75.

[71] Radhakrishnan V, Cristoper P, Singirikonda M, Habibuddin M. Transdermal Drug Delivery Technology a Prospective Review. International Journal of Pharmacy Research & Technology. 2020;10(2):49-73.

[72] Nagdev A, Omprakash A, Rageeb Md, Transdermal Drug Delivery System An Review. Research journal of Pharmacy and Technology. 2022;15(3):1371-1377.

[73] Dangi A. A, Sheth P. Z, Joshi J. Formulation and Evaluation of Transdermal Drug Delivery System. International Journal of Pharmaceutical Research and Allied sciences. 2012;1(2):26-37.

[74] Anirudh B, Mohammed K. Development and Evaluation of Labetalol HCL Matrize Transdermal Patches for the treatment of Hypertension, World journal of Medical Science and Research. 2023;9(12):109- 119.

[75] Saravanakumar K, Swapna P, Nagaveni P, Vani P, Pujitha K, Transdermal Drug Delivery System. Journal of Global Trends in Pharmaceutical Sciences. 2015;6(1):2485-2490.

[76] Patel R, Patel A, Prajapati B, Shinde G, Dharamsi A, Transdermal Drug delivery systems A Review. International Journal of advance Research. 2018;6(5):891-900.

[77] Chinnala M. K, Konda M. A Review on choice of Nicotine Buccal Thin Film for Nicotine Replacement Therapy. World Journal of Medicinal Science and Research. 2017;3(7):96-104.

[78] Ramteke K.H, Dhole S.N, Patil SV. A Review Transdermal Drug Delivery System. Journal of Advanced scientific Research. 2012;3(1):22-35.

[79] Mali D. A, Bathe R, Patil M. An Updated Review on Transdermal Drug Delivery System. International Journal of Advances in scientific Research. 2015;1(06):244-254.

[80] Rotake SB, Hatwar PR, Bakal RL and Kohale NB. Transdermal drug delivery system recent advancements: A comprehensive review, GSC Biological and Pharmaceutical Sciences, 2024; 28(02): 059–072

[81] Pinto L. A, Galan R. C, Gonzalez G. X. Presence of metallic components in transdermal drug delivery systems and risk of skin burn. Farmacia Hospitalaria. 2024:129-132.

[82] Wong Y. F, Chen Y, Huang Y, Cheng C, Transdermal Drug Delivery System for fighting common viral. Infectious diseases. Drug delivery and Translational Research. 2021;11(2):1998-1508.

[83] Khan M, Dangi S. Y. A comprehensive Review on controlled Drug Delivery system Future Directions, World Journal of Pharmaceutics and Medicinal Research. 2023;9(3):158-166.

[84] Tadwer K. I, Gore S, Giradkar P. Advances in topical Drug delivery System A Review. International Journal of pharmaceutical Research and Allied sciences. 2011;1(1):14-23.

[85] Prabahar K, Alanazi Z, Gushawy M, Targeted Drug Delivery System Advantages, carriers and strategies. International Journal of Pharmaceutical Education and Research. 2021;55(2):346-352.

[86] Chavez JJ, Cruz, Delgado, Contreras. Nanocarriers For Transdermal Drug Delivery. Research and Report in Transdermal Drug Delivery. 2012; 1:3-17.

[87] Thakare A, Ahire P, Atkari S, Bade A, Byars V. A Review on Transdermal Drug Delivery system. International Journal of Pharmaceutical Research and Application. 2023;8(3):3457-3467.