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A REVIEW ON TRANSDERMAL PATCH IS AN ADVANCED DOSAGE FORM

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Abstract

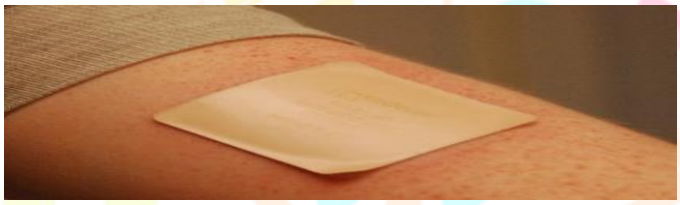
Transdermal therapeutic system are defined as self contained, discrete dosage form which when applied to intact skin deliver the drug through the intact skin at a control rate to the systemic circulation and maintain the drug concentration within the therapeutic window for prolonged period of time In order to deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical, and physicochemical properties of the skin must be considered. Transdermal patches of various varieties are used to introduce active chemicals into the circulatory system through the skin. The transdermal route has several advantages over traditional drug administration routes, including the avoidance of first pass effect, increased bioavailability, patient compliance, painless medication distribution, convenience of application, and removal of the patch in the event of toxicity. Transdermal medication delivery system is a new advanced current novel technology with a bright future, with patches being discovered on a larger scale for their local or topical effect. Drug absorption pathways via the skin are mostly intercellular, intracellular, and trans appendageal. Drug distribution through the skin to provide a systemic effect without causing changes in the drug's plasma concentration. Topical administration of medicinal agents has numerous advantages over traditional oral and invasive medication delivery modalities. In addition, the drug is released in a regulated manner over an extended period of time. The patches have proven to be effective due to significant benefits over previous controlled drug delivery methods. This review article provides a brief overview of the principles of transdermal permeation, various components of transdermal patch, approaches to transdermal patch, evaluation of transdermal system, when transdermal patch should be used and when it should be avoided, and some recent developments in the field, as well as future aspects in this field.

Key words : Transdermal patch,componets of patch,evalution of patches

Introduction:

Transdermal drug delivery devices (TDDS), sometimes known as "patches," are dosage forms designed to transfer a therapeutically effective amount of medicine over a patient's skin. In the creation or discovery of innovative delivery systems, such as transdermal drug delivery, current medication molecules or products not only increase efficacy and safety, but also improve patient compliance and demonstrate the therapeutic effect of a specific medicine.[1] A transdermal medicine delivery system's primary purpose is to release drugs into systemic circulation through the skin at a predetermined rate with minimal variation between and among patients[2].Scopolamine was the first transdermal patch approved by the FDA in 1979 for motion sickness. The second patch was approved in 1981. Now a Several patches are now available in the market for Transdermal application .Patches are typically administered between 1 and 7 days depending on a variety of circumstances [3] Medicated adhesive patches are created in this transdermal delivery technique to transfer therapeutically effective amounts of medication across the skin when placed on the skin. Medicated adhesive patches or transdermal patches come in a variety of sizes and include more than one chemical. When applied to intact skin, they transport active substances into systemic circulation via skin barriers. A patch with a high dose of medicine within that is kept on the skin for an extended period of time and enters the bloodstream via the diffusion process. The drug can enter the skin through three different pathways: hair follicles, sebaceous glands, and sweat ducts. Transdermal medication delivery devices are used to treat a variety of skin illnesses, as well as angina pectoris, pain, smoking cessation, and neurological disorders such as Parkinson's disease.

(Fig.1- Transdermal patch)



Transdermal delivery enables continuous drug input with small intervals, as well as controlled, consistent drug administration. pulsed entrance into biological half-lives and elimination a systemic circulation that frequently has unwanted side effects . Therefore, novel medication delivery systems come in several forms. Methods for transdermal medication administration, controlled relsed system, Trtransmucosal delivery system.[4] Transdermal delivery not only enables controlled, consistent medication administration, but also permits continuous input of pharmaceuticals with short biological half-lives and prevents pulsed entry into systemic circulation, which frequently results in unwanted side effects. As a result, several types of novel drug delivery systems emerged, such as transdermal drug delivery systems, controlled release systems, transmucosal delivery systems, and so on.[5] Transdermal dosage forms, however more expensive than conventional formulations, are gaining popularity due to their distinct advantages. Controlled absorption, more consistent plasma levels, increased bioavailability, decreased adverse effects, painless and uncomplicated application, and the flexibility of discontinuing drug administration by simply removing the patch from the skin are some of the possible benefits of transdermal drug delivery.[6]

Advantages:
• Prevent first-pass gastrointestinal and hepatic metabolism; maintain consistent regulate absorption.[7]
• Patches are simple to use, non-invasive, and painless.[8]
• Patients with gastrointestinal issues can be administered medications via TDDS because there will be no direct contact.
• Contact between the medication and the stomach.
• It provides continuous plasma, just as intravenous infusion.
• If TDDS toxicity develops, the patch can be removed easily.
• It is highly convenient since drug application is quite simple.
• It removes the first pass mechanism.
• It lessens systemic medication interactions.
• It has a long duration of action.
• It is possible to self-administrate.[9]
Disadvantages:
• The medicine, the adhesive, or other excipients in the patch formulation may produce erythema, itching, and local edoema at the site of application.
• Allergic responses are possible.[10]
• Some individuals experience contact dermatitis at the site of application due to one or more system components, necessitating cessation
• Because of the natural restrictions of drug entrance imposed by the skin's imperability, only powerful medicines are appropriate candidates for transdermal patch.
• Some medications, such as scopolamine transdermal patch, are painful to use behind the ear.

Anatomy of skin :

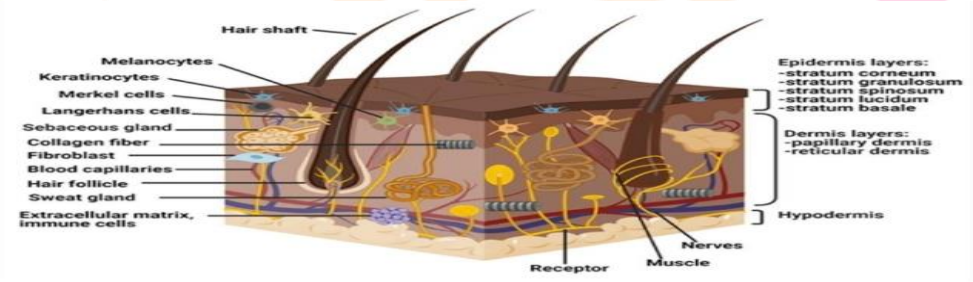
The skin is the biggest an in the human body, and it acts as a permeability barrier to the transdermal absorption of many chemical and biological substances. It is one of the most easily accessible organs of the body, with a thickness ranging from 0.5mm on the eyelids to 4.0mm on the heels of the feet, and it serves as a barrier against physical, chemical, and microbiological threats, as well as acting as a thermostat in maintaining body temperature. Skin has a role in blood pressure regulation and defends against UV light penetration. Skin plays an important role in determining medication delivery features such as penetration and absorption through the dermis. The skin's diffusional resistance is heavily influenced by its anatomy and ultrastructure. The stratified, vascular, cellular "epidermis" underneath the dermis of connective tissues, hypodermis, contains three different yet mutually dependent tissues in human skin.

1.Epidermis

The thickness of the multilayered epidermis varies based on cell size and the number of ad layers of epidermis, ranging from 0.8 mm on the palms and soles to 0.06 mm on the eyelids. The outermost layer of skin, commonly known as the horny layer, is around 10 mm thick when dry but swells to several times this thickness when fully hydrated. It is made up of 10 to 25 layers of dead, keratinized cells known as corneocytes. It is malleable but reasonably impervious. The stratum carenum is the primary barrier to drug entry. A wall-like structure can be used to model the architecture of the horny layer. Keratinized cells in this concept act as protein "bricks" buried in lipid "mortar."

2. Dermis

The dermis is a 3 to 5 mm thick layer of connective tissue that contains blood arteries, lymph vessels, and nerves. The cutaneous blood supply is critical in the control of body temperature. It also nourishes and oxygenates the skin while eliminating impurities and debris. Capillaries reach the skin's surface within 0.2 mm and provide sink conditions for most molecules that penetrate the skin barrier. As a result of the blood supply, the dermal concentration of permeate remains relatively low, and the ensuing concentration gradient across the epidermis provides a critical concentration gradient for transdermal permeation.



(Fig.2 -Anatomy of skin.)

3.Hypodermis

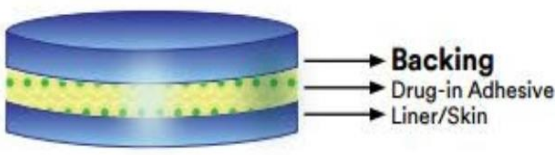
The dermis and epidermis are supported by the hypodermis, or subcutaneous fat tissue. It functions as a fat storage area. This layer aids in temperature regulation, nutritional support, and mechanical protection. It connects major blood veins and nerves to the skin and may house sensory pressure organs. Transdermal drug administration requires drug penetration through all three layers and into systemic circulation, whereas topical medication delivery requires only stratum carenum penetration and drug retention in skin layers.

Types of patches :

1. Single-layer Drug-in-Adhesive :

The drug is also present in the adhesive layer of this system. The adhesive layer of this sort of patch not only helps to glue the numerous layers together, as well as the entire system to the skin, but it is also responsible for medication release. A temporary liner and a backing surround the adhesive layer.[12]

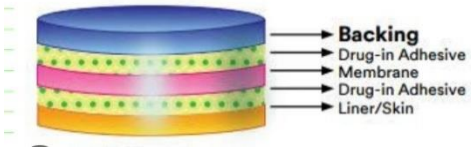
(Fig.3-Single layer drug in adhesive)



2. Multi layer drug in adhesive :

The multi-layer drug-in adhesive patch is similar to the single-layer technology in that both sticky layers are in charge of drug release. The multi-layer system differs in that it adds additional layer of drug-in-adhesive, which is

normally separated by a membrane (though not always). This patch features a temporary liner layer as well as a permanent backing.[13]

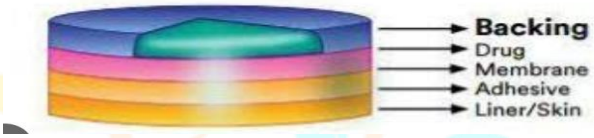


(Fig.4- Multi layer drug in adhesive)

3. Reservoir.

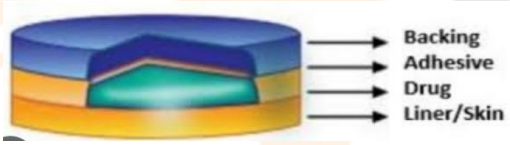
The reservoir transdermal system, unlike the single-layer and multi-layer drug-in-adhesive systems, has a distinct drug layer. The drug layer is a liquid compartment divided by the adhesive layer that contains a drug solution or suspension. The backing layer also supports this patch. The rate of release in this system is zero order.[14]

(Fig.5- Reservoir)



4. The Matrix System

Adhesive system drug The medication reservoir in this type is generated by dispersing the drug in an adhesive polymer and then spreading the medicated adhesive polymer on an impermeable backing layer via solvent casting or melting (in the case of hot melt adhesive). Unmediated sticky polymer films are put to the reservoir's surface for protection.[15]

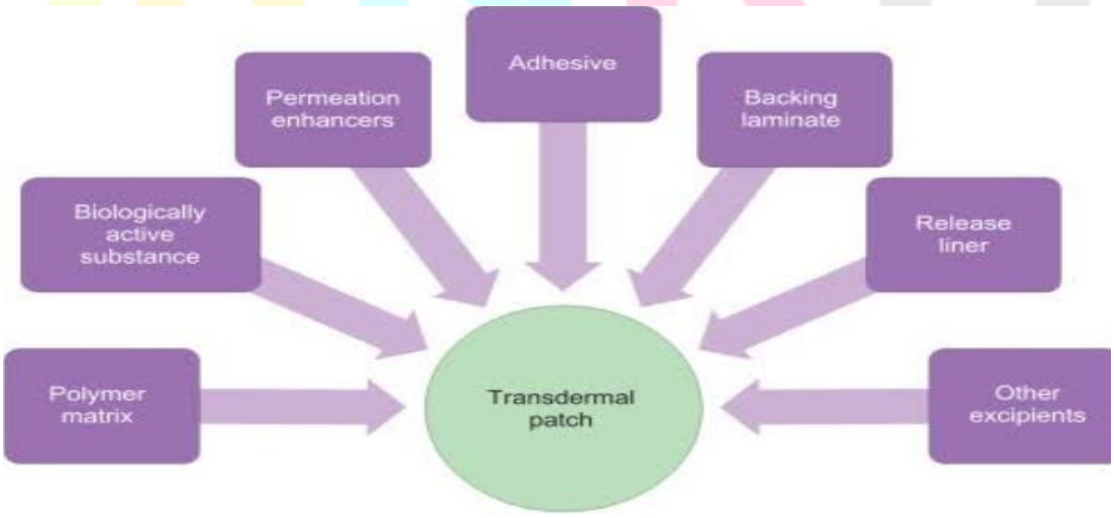


(Fig.6- matrix)

5. Vapour patch:

The job of the adhesive layer in this sort of patch is to not only bind the several layers together but also to release vapour. The vapour patches are new to the market and are often utilised for essential oil release in decongestion. Other types of vapour patches are also available on the market, and they are meant to improve sleep quality and reduce cigarette smoking situations.[16]

Components of patches :



(Fig.7- Components of patches)

1. Drug

The most significant criterion for TDDS is that the medicine has the correct physicochemical and pharmacokinetic properties. Transdermal patches have a lot to offer medications that have a lot of first pass metabolism, pharmaceuticals with a small therapeutic window, or drugs with a short half life that causes noncompliance owing to frequent dosing.

For example, rivastigmine for Alzheimer's and Parkinson's dementia, rotigotine for Parkinson's, methylphenidate for attention deficit hyperactivity disorder, and selegiline for depression have recently been licenced as TDDS.[17]

2.Polymer matrix : These polymers regulate drug release from the drug reservoir. Natural polymers include shellac, gelatine, waxes, gums, starch, and so on.Synthetic polymers include polyvinyl alcohol, polyamide, polyethylene, polypropylene, polyurea, polymethylmethacrylate, and others.[18]

3. Permeation enhancers

Penetration enhancers improve drug absorption by changing the barrier characteristics of the stratum carenum. Penetration enhancers must be non-toxic, non-allergic, pharmacologically inert, flavourless, cheap, and compatible with the drug and excipients. The interaction of intercellular lipids can increase skin permeability by disrupting their cellular organisation and so increasing their fluidity.[19]

4. Adhesive layer:

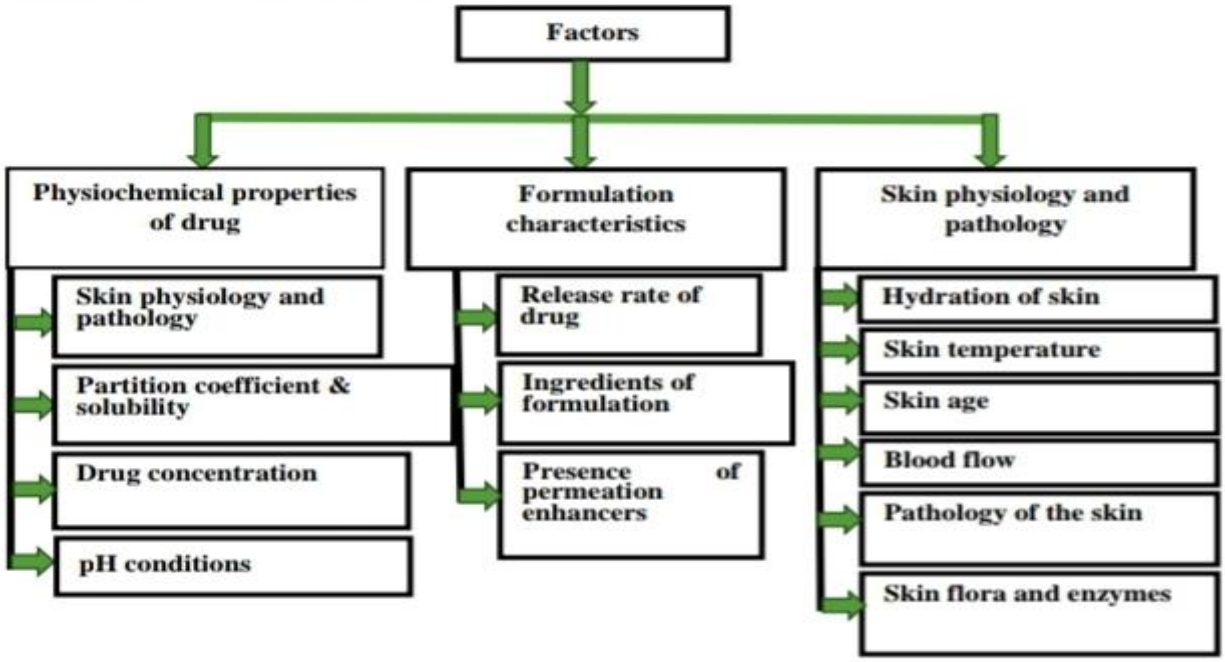
The major function of the adhesive in transdermal patches is to keep the patch in contact with the skin for an extended period of time. Patch selection variables include patch type, patch design, and adhesive qualities. It must be non-irritating, gentle on the skin and excipients, and easy to remove. Silicon-based adhesive polymers, polyacrylate, and polyisobutadiene are some examples of adhesives.[20]

5. Backing laminates

The backing laminate's principal duty is to give support.Because prolonged contact between the backing layer and the excipients may cause the additives to leak out or lead to diffusion of excipients, medication, or penetration enhancer through the layer, the backing layer should be chemical resistant and excipient compatible. They must have a low moisture vapour transmission rate. They must have excellent elasticity, flexibility, and tensile strength.An aluminium vapour coated layer, a plastic film polyethylene, polyvinyl chloride, polyester, and a heat seal layer are some examples of backing materials.[21]

6. Release liner-
   The release liner, which is part of the primary packaging, protects the patch from both drug loss from the polymer matrix and external environment contamination during storage and delivery. It is pulled off before usage. For example, occlusive polyethene or polyvinyl chlorideNon-occlusive (paper fabric)- polyester foil and metallic foil.[22]

Factores affecting Transdermal permiability:



(Fig.8- factors affecting on transdermal patches)

Evaluation of transdermal patch:

1.the patch's thickness

The thickness of the drug-loaded patch is measured at several sites using a digital micrometre, and the average thickness and standard deviation are calculated to ensure the thickness of the created patch.[23]

2.weight uniformity

Before weighing, the patches are dried at 60°C. The patch's weight uniformity is determined by cutting and weighing the 1 cm 2 piece of three patches and then determining the weight variation. The weight of the patch is determined by taking the mean of the three values. Individual weight should not differ much from the average weight.[24]

3.Folding endurance:

A strip of a certain area is cut uniformly and repeatedly folded at the same location until it breaks. The folding endurance value is determined by the number of times the film can be folded at the same location without breaking.[24]

4.Moisture content in percentage

Individually weighed patches are kept in desiccators containing fused calcium chloride at room temperature for 24 hours47,48.After 24 hours, the patches are reweighed, and the percentage moisture content is calculated using the formula: Percentage moisture content = (Initial weight-Final weight/Final weight) x 100[25]

5. Moisture absorption or mass gain

Moisture uptake is commonly represented by mass gain in a transdermal patch. The patch is weighed, placed in a desiccator with a saturated KCl solution, and incubated for up to 24 hours with RH maintained at about 84%. After that, the patch is reweighed, and moisture uptake is estimated using equation.

Moisture uptake (%) =[(Final mass- Initial mass)/Initial mass]×100 [26]

6.Polariscope inspection

This test is used to determine whether the medication is in crystalline or amorphous form. A bit of the patch is placed on the slide and examined to ascertain the physical shape of the drug particles.[27]

7. Tensile Power

A 40 x 15 mm film strip was utilised. When the film was inserted in the film holder, one end of the strip was secured between adhesive tapes to provide stability. Another end of the film was inserted between the adhesive tapes with a tiny pin to maintain the strip straight while stretching. A small hole in the adhesive tape was formed near the pin, and a hook was inserted. To hold the weights, a thread was tied to this hook, passed over the pulley, and a little pin was fastened to the other end. A little pointer was added to the thread, which goes over the graph paper that is attached to the base plate. The film was pulled through a pulley system to assess its tensile strength. To enhance the pulling effort, weights were gradually added to the pan until the film was broken. Break force was defined as the weight required to break the film.[28]

8. Compatibility studies

Compatibility experiments were performed in the current investigation to identify any incompatibility between the medication and polymers. The IR studies were carried out to ensure compatibility with excipients. The potassium bromide pellet approach was used to collect spectra of the pure medication and the prepared patch separately.[29]

9.Flatness

A transdermal patch should have a smooth surface and not constrict over time. This is proved through a flatness research. To determine flatness, one strip is cut from the middle and two from each side of the patches. The length of each strip is measured, and the variance in length is determined by calculating the percent constriction. Zero percent constriction is equal to 100 percent flatness.

%Constriction =(I_1-I_2/I_1)×100

I_2 = Final length of each strip

I_1 = Initial length of each strip [30]

10.Peel adhesion test

This test calculates the force required to remove a patch from a surface. The patch is put to the surface of a steel plate and is pushed away at an angle of 1800 degrees from the surface. The force required to remove the patch is measured.[31]

11.Water vapour permeability :

Water vapour permeability can be tested using the foam dressing method, in which an air forced oven is replaced by a natural air circulation oven. The following formula can be used to calculate the WVP.

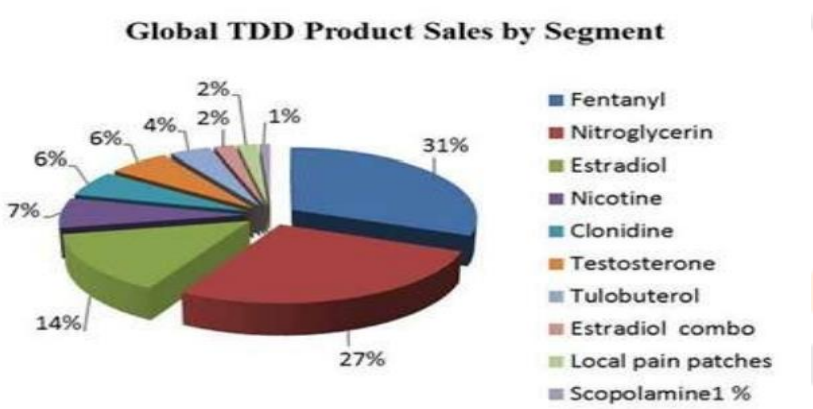
WVP=W/A

Where WVP is indicated in gm/m2 per 24 hours, W is the quantity of vapour permeated through the patch stated in gm/24 hours, and A is the surface area of the exposure samples ePrakash Pasupuleti, kishore Bandara palle, herlopalli Bandhya, Gundam Neeraja, Chikkala, TA AF201 Chithrala Venkataramana Golla venkat sai. Pasupuleti et at Transdermal drug delivery systems. Pasupuloti et al Journal of doug delivery of Therapeutics 2008; 18(2): 101-199xpressed in m^2 [32]

Statistically application of tdds:

The use of transdermal drug delivery systems has expanded in India and around the world because to their safety, efficacy, and convenience, as well as their low rejection rate. It is the most appealing method. It is commonly utilised due to the regulated release of medicines.1.A graphical representation of global TDD product sales by segment is seen below.Fentanyl has the greatest percentage (31%), followed by nitroglycerin (27%), estradiol (14%), nicotine (7%), clonidine (6%), testosterone (6%), tulobuterol (4%), estradiol combination (2%), local pain patches (2%), and scopolamine

(Fig.9- Tdd products)



Challenges and Future Prospects:

TDD is a non-invasive delivery method that is generally regarded as simple to administer, even in more vulnerable age groups such as paediatric and geriatric patients, while avoiding some bioavailability concerns that arise from oral drug delivery due to poor absorbability and metabolism concerns. The skin's large surface area and accessibility make it a convenient and patient-friendly medication delivery target. The elimination of first-pass metabolism, steady distribution, enhanced patient compliance, fewer systemic medication interactions, sustained drug release, and overall greater therapeutic efficacy are all important advantages of transdermal delivery. Despite this great increase, there are still significant barriers that limit the use of TDD to a few medications. Only a few medications using chemical TDD methods have been successfully commercialised. Chemical TDD systems, such as niosomes and nanocrystals, are not the final dosage forms and must be transformed into a suitable dosage form (i.e., patches, creams, gels, etc.) before usage. The addition of excipients, which are required for various dosage forms, raises the cost and complexity of the manufacturing process while also introducing several points of failure, such as particle size optimisation and drug leakage concerns, which must be tightly controlled to avoid lowering efficacy.[33]

Conclusion:

Transdermal drug delivery systems are used in medicine therapy to achieve reduced absorption, more uniform plasma levels, greater bioavailability, fewer adverse effects, effectiveness, and product quality. A patch is made up of a few fundamental components that play a vital role in medicine release via the skin. The future of TDDS would be centred on regulated therapeutic usage. There are

many different types of transdermal patches, including matrix, reservoir, membrane matrix hybrid, micro reservoir type, and medication in adhesive type. The basic TDDS components are used to create Transdermal patches from these patches.

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