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STICK TO IT: A COMPREHENSIVE REVIEW OF TRANSDERMAL PATCH TECHNOLOGY

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ABSTRACT
An innovative way to medication distribution, transdermal patches provide a regulated, non-invasive, and patient-friendly substitute for conventional techniques. Transdermal patch technology is thoroughly reviewed in this article, which also examines its fundamental ideas, essential elements, and many medical treatment uses. Advances in adhesive and matrix technologies, the mechanics of medication absorption via the skin, and methods for overcoming obstacles such skin irritation and restricted permeability are among the topics discussed. Recent advancements including smart patches with real-time monitoring features and patches augmented by microneedles are also highlighted in the review. The potential of transdermal patches to transform healthcare delivery and open the door to more effective and individualized treatment solutions is highlighted in this article by discussing both the advantages and disadvantages of this technology.
KEYWORDS: *Transdermal patches, TDDS, Enhancer for Permeation, Folding endurance, permeability.*

1. INTRODUCTION

Through the use of a special membrane, a patch of transdermal —also called to as a patch of skin—it controls the rate at which the medication in the liquid form in the reservoir inside the transdermal patch can pass through the skin and into the blood stream. For few medications to be utilised in a skin patch, they must be mixed with substances that improve their penetration of the skin, including alcohol. Medications that are applied as skin patches include nitro-glycerin (for angina), nicotine (for quitting smoking), oestrogen (for menopause and to prevent osteoporosis after menopause), lidocaine (for shingles pain; herpes zoster) and scopolamine (for motion sickness).However, some chemicals, like molecules of insulin, are very big to fit by way of the epidermis. Applying transdermal patches to the skin removes the need for pumps or syringes to gain vascular entry. In the 1970s, these patches were created, and the FDA authorised the first one in 1979 to cure motion sickness.[1, 2].Delivering a amount of therapeutically effective medication through the skin of patient is the aim of TDDS(transdermal drug delivery systems) [3–4].
Traditional drug regimens that call for many doses have a lot of issues and side effects; include less bioavailability because of first pass metabolism of hepatic. TDDS takes this away. For these medications, the aim of dosage design is to optimise the flow of medication into the systemic circulation through the skin while reducing metabolism in the skin and drug retention [5]. Self-contained, discrete dose forms known as TDDS (transdermal drug delivery systems) can be used to healthy skin to allow the drug or drugs to enter the bloodstream at a regulated pace. Transdermal administration is acknowledged as a viable method for both local and systemic medication delivery [6]. TDDS not only allows for the drug of continuous injection with short biological half lives but TDDS also avoids pulsed entry into the bloodstream, which often leads to undesirable side effects. It also provides consistent, controlled drug administration. Novel medication delivery approaches have emerged, including transdermal drug administration methods, controlled release system and transmucosal drug delivery systems [7].

1.1 Definition

A transdermal patch or skin patch also called as medicated adhesive patch is applied to the skin for the purpose of deliver a specific medication amount into the bloodstream through the skin. [8]

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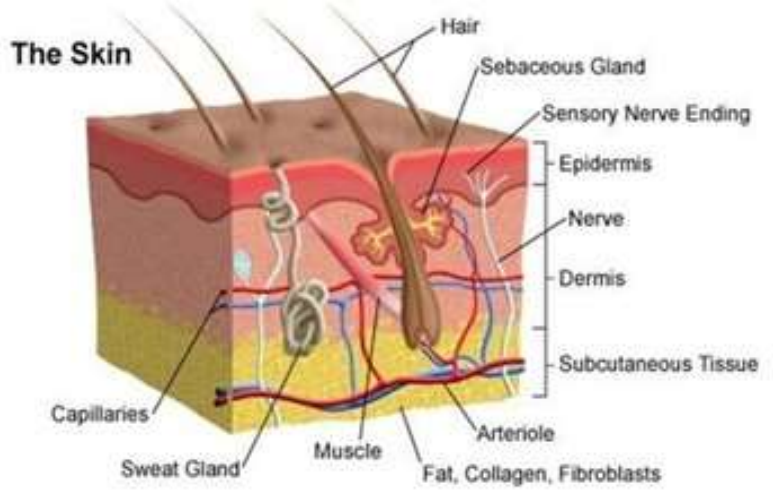

Figure 1. Structure of skin for transdermal drug delivery systems

2. TRANSDERMAL DRUG DELIVERY ADVANTAGES [9-14]

1. TDDS is a system of drug delivery that applies a gadget, which is called a patch, to the surface of skin enters into the systemic circulation at a predetermined concentration for therapeutic advantage. This prevents other restrictions brought on by another dosage forms.
2. TDDS provides consistent drug penetration through the skin, resulting in a steady serum drug level, which is the therapeutic objective.
3. For patients who have trouble taking medications orally, It can be used in place of the oral drug administration method.
4. Patients who are unconscious or feel queasy can use it as an alternative.
5. Since there won't be any direct drug delivery, patients with gastrointestinal issues can receive medication through TDDS.

3. DISADVANTAGES

1. Because of one or more than one system components, some of the patients develop contact dermatitis at the site of application, necessitating treatment discontinuation.
2. Because the skin's imperability naturally limits drug entrance, these patches are only appropriate for drugs which are powerful.
3. Few medications are painful, such as the transdermal patch of scopolamine, which is applied behind the ear.
4. Adhering for a long time is challenging. [15, 16]

4. TRANSDERMAL PATCH: [17-20]

To deliver the specific medication quantity into the bloodstream through the skin at a predetermined rate of release, a adhesive medicinal patch (transdermal patch) which is put to the skin above the epidermis. The most popular transdermal technology available today is mostly based on patches, which are semi-permeable membranes. A TDDS (transdermal drug delivery system), often known as "transdermal patches" and "skin patches," is therapeutically effective dose form that is meant to be injected into a patient's bloodstream through their skin.

Figure 2. Structure of Transdermal Patch

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5. APPLICATIONS OF TRANSDERMAL PATCHES [37-39]

• The patch of nicotin, which helps people quit smoking tobacco by releasing nicotine in controlled dosages, so it is the most famous transdermal patch in the US.
•Two opioid drugs, buprenorphine (marketed as BuTrans) and fentanyl (marketed as Duragesic), are frequently administered in patch form to treat extreme pain 24/7.
• Menopausal symptoms and postmenopausal osteoporosis are occasionally treated with oestrogen patches. The patch of contraceptive (also known as Ortho Evra or Evra) is another transdermal patch for hormone delivery.

6. TRANSDERMAL PATCHES' CONSTITUENT PARTS

1. Matrix of Polymers: The polymer regulates the release of drug from the device. To be used in the transdermal patches, a polymer must meet the following requirements.
Types of polymers include:
a) Natural polymers: which include starch, gum, shellac, proteins, gelatin, cellulose derivatives, and waxes.
b) Artificial Elastomers: Neoprene, Nitrile, Acrylonitrile, Hydrin Rubber, and Silicone Rubber.
c) Synthetic polymers: include epoxy, polyvinyl chloride, polyvinyl alcohol, polypropylene, polyethylene, polyamiode, and polyurea.

2. Drug: -The solution of drug in close proximity to the release liner.
Physiochemical Characteristics
a) The medication's molecular weight should be under 1000 Daltons.
b) Both lipophilic and hydrophilic phases should be favoured by the medication.
c) The drug's melting point should be low.

3. Enhancer for Permeation: The flow of the drug J. can be inscribed through the skin. Given that

$$J = D\, dc/dx,$$

J represents the flux.
D is an acronym for diffusion coefficient.
C represents the concentration of the diffusing spectrum.
X is a coordinate in space.

4. Extra excipients: (a) Adhesives: The device's face or back can be covered with the pressure-sensitive adhesive.
i) It must not cause irritation.
ii) It must removedsimply.
iii) It shouldn't leave behind any residue that is impossible to wash off.
iv) It must have superior skin contact.
v) Compatibility with the drug both chemically and physically.
vi) Drug penetration shouldn't be impacted.

5. Linear: - Protect the patch during the time of storage. The linear is removed before to usage.

6. Backing: - Shield the transdermal patch from the weather. [21–30]

7. Elements that influence transdermal bioavailability [31–36]
The drug's transdermal bioavailability is influenced by two main factors:
1. Physicochemical Elements
(a) Hydration of the skin: When the skin and water comes in touch, its permeability increases crucial element boosting skin penetration is hydration. Thus, transdermal delivery is the method used to apply humectant.
(b) pH and temperature: Changes in pH cause a tenfold increase in medication penetration. When the temperature decreases, the diffusion coefficient also decreases. How weak bases and weak acids separate is determined by the pKa or pKb and pH values. The unionised drug's percentage in the skin indicates the concentration of drug. Therefore, two crucial variables influencing medication penetration are pH and temperature.

2. Aspects of Biology
(a) Skin condition: Many solvents, including methanol and chloroform, as well as acids and alkalis, harm skin cells and encourage penetration. Skin conditions change when a patient is ill. Although healthy skin provides a better barrier, penetration is impacted by the aforementioned factors.
(b) Skin age: Younger skin has a higher permeability than older skin. Children are especially susceptible to pollutants absorbing via their skin. Therefore, skin age a main parameters that affect penetration of medication in transdermal drug delivery system.

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8. EVALUATION METHODS: [40–51]

1. Patch thickness: Using a digital micrometre, the thickness of the drug-loaded patch is measured at various spots. The average thickness and standard deviation are then calculated to guarantee the thickness of the created patch.

2. Weight uniformity: Before testing, the produced patches must be dried for four hours at 60°C. A predetermined patch area must be sliced into several sections and weighed using a digital balance. From the individual weights, the average weight and standard deviation values must be computed.

3. Folding endurance: a strip of a particular material has to be cut uniformly and folded repeatedly until it breaks. The folding endurance was determined by counting the number of times the film could be folded in the same spot without breaking.

4. The percentage Content of moisture: Each manufactured film must be weighed separately and stored in a desiccator. keeping fused calcium chloride for a whole day at room temperature. The films must be reweighed after a day in order to calculate the moisture content as a percentage using the formula below.

Percentage moisture content = [Initial weight- Final weight/ Final weight] ×100.

5. Moisture uptake percentage: To maintain 84% relative humidity, the weighted films must be stored at room temperature for 24 hours in a desiccator filled with a saturated potassium chloride solution. Following a 24-hour period, the films must be reweighed in order to calculate the percentage moisture uptake using the formula below.

Percentage moisture uptake = [Final weight- Initial weight/ initial weight] ×100.

6. Drug content: A predetermined patch area needs to dissolve in a predetermined volume of an appropriate solvent. After passing the solution through a filter medium, the drug content must be examined using the appropriate technology (either the UV or HPLC method). The average of three separate samples is shown by each value.

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