TRANSDERMAL DRUG DELIVERY TECHNOLOGY
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ABSTRACT
Transdermal drug technology specialists are continuing to search for new methods that can effectively and painlessly deliver larger molecules in therapeutic quantities to overcome the difficulties associated with the oral route. TDDS is developed in three generations such as: first-generation, second-generation, third-generation. The patches have been proved effective because of its large advantages over other controlled drug delivery systems. This review article covers a brief outline of various components of transdermal patch, applications of transdermal patch, their advantages, disadvantages, when the transdermal patch are used and when their use should be avoided.

KEY WORDS: Transdermal drug delivery, First, Second and third generation.

1. INTRODUCTION (SHRIERAJ SHAH, 2008)
A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream.

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied creams and ointments for dermatological disorders. (Shrierraj shah, 2008) The occurrence of systemic side-effects with some of these formulations is indicative of absorption through the skin. Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation, it overcomes various side effects like painful delivery of the drugs and the first pass metabolism of the drug occurred by other means of drug delivery systems. So, this Transdermal Drug Delivery System has been a great field of interest in the recent time... A Transdermal Patch has several components like liners, adherents, drug reservoirs, drug release membrane etc. The first commercially available prescription patch was approved by the U.S. Food and Drug Administration in December 1979, which administered scopolamine for motion sickness.

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Generation of transdermal delivery systems (Mark R. Prausnitz, 2008.)

Transdermal system design
Patch design is among the first considerations in developing a transdermal drug. Properties of the drug, the desired delivery profile, and the target patient group determine which design is best for a given application (Morgan, 1998; Foldvari, 2006).

Every design incorporates four elements:
- A backing
- An adhesive
- A release liner
- The drug

The reservoir and multilaminate designs include a membrane film that controls the rate of delivery from the patch. In the reservoir-type design, the drug solution is in a liquid reservoir compartment, separated from the release liner by a semipermeable membrane and an adhesive.

The matrix design is similar to that of the reservoir, but the drug was provided as a semisolid formulation and there is no membrane layer. Drug-in-adhesive (DIA) transdermal systems incorporate the drug directly within the skin contacting adhesive.
A multilaminate DIA design adds a membrane between two distinct DIA layers or multiple DIA layers under a single backing. Because of its elegant simplicity and patient preference, DIA is considered state-of-the-art in transdermal drug delivery systems design.

The simple appearance of a transdermal drug delivery patch belies the complex development process necessary to produce a therapeutically effective patch. There is no single "recipe" that applies to every transdermal drug delivery product.

**Components of Transdermal Patch**
- **Liner** - Protects the patch during storage. The liner is removed prior to use.
- **Drug** - Drug solution in direct contact with release liner.
- **Adhesive** - Serves to adhere the components of the patch together along with adhering the patch to the skin (Smith, 2006).
- **Membrane** - Controls the release of the drug from the reservoir and multi-layer patches.
- **Backing** - Protects the patch from the outer environment.

**Factors affecting transdermal bioavailability** (Shreeraj shah, 2008)
- Two major factors affect the bioavailability of the drug via transdermal routes:
  - **Physiological factors**
  - **Formulation factors**

**Physiological factors include**
- Stratum corneum layer of the skin
- Anatomic site of application on the body
- Skin condition and disease
- Age of the patient,
- Skin metabolism
- Desquamation (peeling or flaking of the surface of the skin)
- Skin irritation and sensitization (7 Race

**Mechanism of Transdermal Patch Action**:- 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 (Mayes, 2006).

**Iontophoresis**:- Iontophoresis passes a few milliamperees of current to a few square centimeters of skin through the electrode placed in contact with the skin.

**Application by ultrasound**:- Application of ultrasound, particularly low frequency ultrasound, has been shown to enhance transdermal transport of various drugs including macromolecules. It is also known as sonophoresis, reported on the use of low-frequency sonophoresis for topical delivery of EMLA cream.

**Use of microscopic projection**:- Transdermal patches with microscopic projections called microneedles were used to facilitate transdermal drug transport. Needles ranging from approximately 10-100 μm in length are arranged in arrays. When pressed into the skin, the arrays make microscopic punctures that are large enough to deliver macromolecules, but small enough that the patient does not feel the penetration or pain. The drug is surface coated on the microneedles to aid in rapid absorption. They are used in development of cutaneous vaccines for tetanus and influenza. Various other methods are also used for the application of the transdermal patches like thermal poration, magnetophoresis, and photomechanical waves (chin).

**Types of Transdermal Patch**
- **Single-layer Drug-in-Adhesive**:- The adhesive layer of this system also contains the drug.
In this type of patch the adhesive layer not only serves to adhere the various layers together, along with the entire system to the skin, but is also responsible for the releasing of the drug. (Guy, 2003) The adhesive layer is surrounded by a temporary liner and a backing.

**Multi-layer Drug-in-Adhesive:** The multi-layer drug-in-adhesive patch is similar to the single-layer system in that both adhesive layers are also responsible for the releasing of the drug. The multi-layer system is different however that it adds another layer of drug-in-adhesive, usually separated by a membrane (but not in all cases). This patch also has a temporary liner-layer and a permanent backing.

**Reservoir:** Unlike the Single-layer and Multi-layer Drug-in-adhesive systems the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the adhesive layer. This patch is also backed by the backing layer. In this type of system the rate of release is zero order.

**Matrix:** The Matrix system has a drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlaying it.

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

**Conditions in which Transdermal Patches are used**

Transdermal patch is used when (Williams, 2004)

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

- It can be used in combination with other enhancement strategies to produce synergistic effects

**Conditions 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 and
- Where requirement of dose is equal to or less than 30 mg/24 hrs.

**Marketed Products of Transdermal Patches:**

(Shreeraj Shah, 2008)

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Drug</th>
<th>Manufacturer</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotinell®</td>
<td>Nicotine</td>
<td>Novartis</td>
<td>Pharmacological smoking cessation</td>
</tr>
<tr>
<td>Matrifex®</td>
<td>Fentanyl</td>
<td>Nycomed</td>
<td>Pain relief patch</td>
</tr>
<tr>
<td>Ortho Evra®</td>
<td>Nedolestramin/Ethiny Estradiol</td>
<td>ORTHO-McNEIL</td>
<td>Postmenstrual syndrome</td>
</tr>
<tr>
<td>NuPatch 100</td>
<td>Diclofenac diethylamine</td>
<td>Zydus Cadila</td>
<td>Anti Inflammatory</td>
</tr>
</tbody>
</table>

**Care taken while applying transdermal patch**

- The part of the skin where the patch is to be applied should be properly cleared.
- Patch should not be cut because cutting the patch destroys the drug delivery system.
- Before applying a new patch it should be made sure that the old patch is removed from the site.
- Care should be taken while applying or removing the patch because anyone handling the patch can absorb the drug from the patch.
- The patch should be applied accurately to the site of administration.

**Recent research done in the field**

Number of research works are going on in this field. Few of the latest research done in the field of transdermal patches are stated below:

**Pain-free diabetic monitoring using transdermal patches:** The first prototype patch measures about 1 cm² and is made using polymers and thin metallic films. The 5×5 sampling array can be clearly seen, as well as...
their metallic interconnections. When the seal is compromised, the interstitial fluid, and the biomolecules contained therein, becomes accessible on the skin surface.

**Testosterone Transdermal Patch System in Young Women with Spontaneous Premature Ovarian Failure:** In premenopausal women, the daily testosterone production is approximately 300 μg, of which approximately half is derived from the ovaries and half from the adrenal glands. Young women with spontaneous premature ovarian failure (sPOF) may have lower androgen levels, compared with normal ovulatory women. Testosterone transdermal patch (TTP) was designed to deliver the normal ovarian production rate of testosterone. The addition of TTP to cyclic E2/MPA therapy in women with sPOF produced mean free testosterone levels that approximate the upper limit of normal.

**Other Research Works going on In This Field**
- Transdermal Patch of Oxybutynin used in overactive Bladder.
- Transdermal Patch (Ortho Evra™)
- Rotigotine transdermal patch

**2. CONCLUSION**

A lot of progress has been done in the field of Transdermal Patches. Due to large advantages of the Transdermal Drug Delivery System, this system interests a lot of researchers. Many new researches are going on in the present day to incorporate newer drugs via this system. Various devices which help in increasing the rate of absorption and penetration of the drug are also being studied. However, in the present time due to certain disadvantages like large drug molecules cannot be delivered, large dose cannot be given, the rate of absorption of the drug is less, skin irritation, and etc. the use of the Transdermal Drug Delivery System has been limited. But, with the invention of the new devices and new drugs which can be incorporated via this system.

**REFERENCES:**


Smith EW.; Maibach HI, editors, Percutaneous Penetration Enhancers Boca Raton FL, Taylor and Francis Group, 2006.