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Transdermal Patch: A Comprehensive Overview of Newer Drug Delivery System in Modern Medical Science

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Abstract
Background: *Oral route of drug administration has been the most common route of drug administration since the beginning of the therapeuticarea in medical science. However this route of drug administration fails at bypassing the first pass metabolism of the drug in liver with poor bio availability. Oral route of drug administration also fails in uncooperative /unconscious semiconscious / pediatric subjects. Transdermal patch, a new drug delivery system through skin to the parenteral circulation has been the most recently discussed topic in pharmacology and medicine as it is a noninvasive route of drug administration, delivered in a sustained / pre fixed dosage with no / extremely less first pass metabolism and better bio availability. Most importantly it can be used in semiconscious / unconscious & pediatric subjects without affecting their hemodynamics. The transdermal patches have many beneficial factors however they also come with some major drawbacks like varieties of formulation, design and quality of adhesiveness. This articles provides an insight of transdermal patch in terms of its mechanism of action, advantages, disadvantages and future scope of it in the medical science.*
Keywords: *drug, transdermal patch,Bioavailability.*

Introduction

Man and the disease have been intimate to each other since the beginning of human evolution. As the lifestyle and habits changed from simple to complex the mankind has been witnessingmany more number of diseases in various presentations; accordingly various molecules / drugs have been discovered with many attempts in delivering it in different routes. The oral route of drug administration is the most accepted among all with about two third of the medications products delivered through this route.

Poor absorption rate, rapid first pass metabolism in liver with significant low bio availability of the drug and prominent gastro intestinal adverse reactions makes oral route not a much recommended route of drug administration in current scenario.

Since the beginning of civilization human beings have applied a lot of substances on the skin as a cosmetic / therapeutic agent however it was in the 19th century skin (Transdermal route) became the preferred route of administration for the long term drug delivery [(1)].

A transdermal patch can be defined as "A medicated adhesive patch which is placed over the skin to deliver a specific dose of medication through the skin with predetermined rate of release to reach in to the blood stream". [1]

A transdermal patch comes in various size, shape, colour and thickness with many layers in it. Depending on the drug, the patches generally last from one to seven days.

Transdermal patches were developed inthe 1970s and the first transdermal patch was approved by the FDA in 1979 for the treatment of motion sickness. In 1981, patches for nitroglycerinwere approved in the treatment of cardiac diseases and today there exist a number of transdermal patches in the treatment of many diseases. Drugs like clonidine, fentanyl, lidocaine, nicotine, nitroglycerin, oestradiol, oxybutinin, scopolamine, and testosterone are delivered via transdermal patch in the treatment of many diseases [2]

These days the Transdermal patches have been the most preferred route of drug administration for hormone replacement therapy and infertility.

Mechanism of Action

A typical transdermal patch consists of an adhesive layer which sticks on to the skin, a semi solid to liquid drug is smeared between the layers of drug releasing membranes which are exclusively semipermeable in nature. An outermost clear baking protects overall patch during application.

A transdermal patch when applied to skin, establishes a good connection between the skin and semi permeable membrane. A slow a sustained flow of drug occurs from drug reservoir of the patch to the skin via drug release membrane by simple diffusion/ osmosis process through percutaneous drug delivery system.

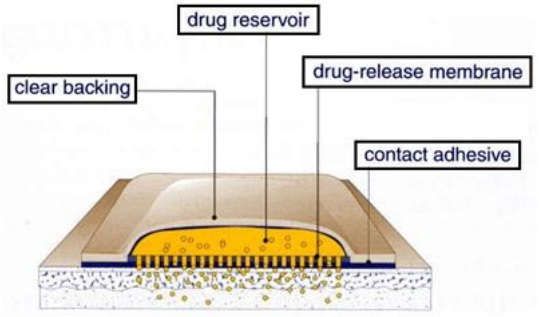


Diagram showing the different layers of transdermal patch with mechanism of action [3]

There are numerous dermal patches are available in different size, shape, layers and thickness for the therapeutic usages. Some of the important therapeutic transdermal patches with their key drug / molecule and primary indication for the usage is listed below [4],

Table 1.1 featuring different transdermal patches, its brand name, molecule and indecation

Brand name	Key drug / molecule	Indication
Estraderm	Estradiol	Postmenstrual Syndrome
Duragesic	Fentanyl Reservoir Pain relief patch	Pain operative neuralgia
Transdermscop	Scopolamine	Motion sickness
Deponit	Nitroglycrine	Angina pectoris
Lidoderm	Lidocaine	Drug in adhesive Anaesthetic (postoperative pain relief)
Testoderm	Testosterone Reservoir	Hypogonadism in males
Emsam	Selegiline	Depression & mood disorder
Nicoderm CQ	Nicotine	Rehabilitation in chronic smokers

Advantages

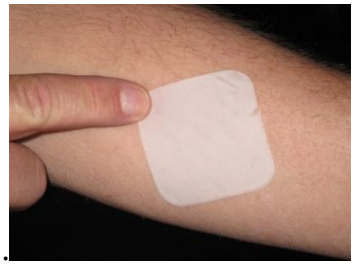
Following are the advantages of transdermal patches,

1. Transdermal patches are easier to apply and remove hence they are user / patient friendly [(1)].
2. They can be comfortably used in elderly, mentally retarded subjects and pediatric age groups without the risk of over dosage and adverse effects.
3. Dermal patches are relatively painless and completely noninvasive which makes them the first choice of selection for chronically ill patients
4. Transdermal patch is the best route of drug administration for those drugs which gets broken down by gastric juice, poor absorption in gut and the drugs with short lifespan (e.g. hormones & peptides) [(5)].
5. Dermal patches avoid the first pass metabolism in liver to a very significant extent thus providing a greater bioavailability to the body.
6. The dosage of the drug is significantly reduced due to greater bioavailability to the body hence even a small dose of drug is sufficient enough to bring the pharmacological actions.
7. Dermal patch also provide the sustained release of drug with constant plasma values which provides the longer duration of action [(5)].
8. This mode of drug delivery provides very less adverse effects (nausea, vomiting, gastritis, bowel disturbances) & parenteral hazards (blood borne infections, pain & swelling at the site of injections) when compared to that of oral and parenteral route of drug administration.
9. The drug administration (input) can be terminated at any point of time by removing the patch thus eliminating the risk over dosage & related complications [(4)].
10. Transdermal patches are cost effective with longer duration of pharmacological action. Hence it minimizes the economical burden on the patient to a greater extent.
11. Transdermal patches are best alternative choice for those chronic (prolong bed ridden, comatose and patients with old age and memory issues) patients who does not like taking the medications orally / parenterally with many medications in multiple frequencies in a day [(1)]
12. It also proves very safe and handy in serving the patient in emergency situations like accidents, poisoning, unconscious and semiconscious patients.

Disadvantages

1. Skin being the outermost protective organ of the body with hydrophobic (water resistant) property. Hence the drugs with hydrophilic property cannot be delivered through transdermal patch and transdermal patches also fail in delivering the skin irritant drugs. This is one of the major disadvantage of the transdermal route of drug delivery system [(5)].
2. Dermal patch serves the best in delivering thedrug at the rate of < 5mg of molecule / day. Itslower down significantly in case of drug dosage delivery of about 10 – 25mg/ day and beyond 25 mg/ day the transdermal patches fail to deliver the drug. Hence this drug delivery system cannot be used in cases demanding high level of drug dosage maintenance in blood for longer periods [(1)].
3. Drugs with larger molecule size more (>1000 dalton) cannot be delivered through transdermal route of drug administration [(1)].
4. The drugs in anionic forms are best delivered through dermal patches however the drugs in ionic form fail to deliver through this route [(2)].

5. Contact dermatitis is one of the commonest local adverse reaction observed with local erythema, itching and swelling at the site of application being the minor and frequently observed adverse reactions in this drug delivery system [4]



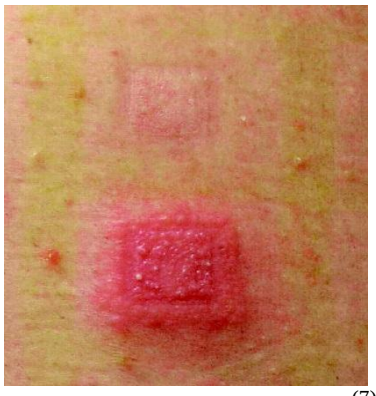


Fig. 2: Transdermal Patch on application [7] Fig 3: Local Induration at the Application Site [6]

6. The barrier system of the skin changes from one site to another, from individual to individual with respect to age hence choosing the right site of adhesion in appropriate age group is also important in effective drug delivery [5].

7. The quality of adhesiveness, size, design, thickness of the patch, lack of technical and manufacturing skills also play as a hindrance in this transdermal route of drug delivery system.

Conclusion

Transdermal route of drug delivery system has been one of the advanced mode of drug delivery with safety and good efficacy. There have been lot of improvement in the process of transdermal route of drug delivery since its beginning years of 1981 to the current advancements in 2016.

An easy process of application and removal, prolonged period of action in pre-defined doses as desired with good plasma value maintenance of the dose makes it very popular route of drug administration. It has more patient acceptance due to low price, excellent pharmacological action in low doses with significant reduction in GI adverse events.

However it fails in delivering the ionic form of drugs and hydrophilic molecules with some of the manufacturing issues which involves thickness, size, adhesive property and other minor processing issues.

With a little advancement in its manufacturing process and drug delivery system transdermal patch can prove out to be the most recommended route of drug administration in the near future. Especially for a developing country like India with high incidence of non-communicable disorders (Diabetes mellitus, stroke, systemic hypertension and associated cardiac disorders) transdermal route of drug administration can be a real boon to the patient with significant reduction in the socio economic burden in community.

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