

## USE OF TRANSDERMAL PATCHES AS DRUG DELIVERY SYSTEM: GLOBAL SCENARIO

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Article Received on  
09 Jan 2014,

Revised on 03 Feb 2015,  
Accepted on 28 Feb 2015

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### **ABSTRACT**

Transdermal drug delivery system is topically administered medicaments. Transdermal patches are pharmaceutical preparation of varying sizes, containing, one or more active ingredient, intended to be applied to the unbroken skin in order to deliver the active ingredient to the systemic circulation after passing through the skin barriers, and to avoid first pass effect. 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. Since there is high concentration on the patch and low concentration in the blood, the drug will keep diffusing into the blood, for a long period of time, maintaining the constant concentration of

drug in the blood flow. Characterization of transdermal patch is done to check its quality, size, time of onset & duration, adhesive property, thickness, weight of patch, moisture content, uniformity & cutaneous toxicological studies. The market for transdermal products has been in a significant upward trend that is likely to continue for the foreseeable future. An increasing number of TDD products continue to deliver real therapeutic benefit to patients around the world. More than 35 TDD products have now been approved for sale in the US, and approximately 16 active ingredients are approved for use in TDD products globally.

**KEYWORDS:** TDD products, Transdermal, predetermined and controlled rate.

### **INTRODUCTION**

The most common, form of delivery of drugs is the oral route. It has the notable advantage of easy administration, but also has significant drawbacks – namely poor bioavailability due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both

high and low), leading to a need for high and / or frequent dosing, which can be both cost prohibitive and inconvenient. To overcome these difficulties there was a need for the development of new drug delivery system; which can improve the therapeutic efficacy and safety of drugs by more precise spatial and temporal placement within the body thereby reducing both the size and number of doses. Transdermal drug delivery system are topically administered medicaments, in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. Transdermal patches are flexible pharmaceutical preparation of varying sizes, containing, one or more active ingredients. They are intended to be applied to the unbroken skin in order to deliver the active ingredient to the systemic circulation after passing through the skin barriers. Theoretically, transdermal patches works in a very simple way. A drug is applied in a relatively high dosage to the inside of patch, which is worn on the skin for an extended period of time. Though a diffusion process, the drug enters the bloodstream directly through the skin. Since there is high concentration on the patch and low concentration in the blood, the drug will keep diffusing into the blood, for a long period of time, maintaining the constant concentration of drug in the blood flow.

Thus 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.



### Advantages

1. They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH, enzymatic activity, and drug interactions with food, drink, and other orally administered drugs.
2. They can substitute for oral administration of medication when that route is unsuitable, as with vomiting and diarrhoea.

3. They avoid the first-pass effect, that is, the initial passage of drug substance through the systemic and portal circulation following gastrointestinal absorption, possibly avoiding the deactivation by digestive and liver enzymes.
4. They are non invasive, avoiding the inconvenience of Parenteral therapy.
5. They provide extended therapy with a single application, improving compliance over other dosage forms requiring more frequent dose administration.
6. The activity of drugs having short half-life is extended through the reservoir of drug in the therapeutic delivery system and its controlled release.
7. Drug therapy may be terminated rapidly by removal of its application from the surface of the skin.
8. They are easily and rapidly identified in emergencies (for example, unresponsive, unconscious patient) because of their physical presence, features, and identifying markings.

### **Disadvantages**

1. Some patients develop contact dermatitis at the site of application from one or more of the system components, necessitating discontinuation.
2. The delivery system cannot be used for drugs requiring high blood levels.
3. The use of transdermal delivery may be uneconomical.

### **FORMULATION DESIGN**

A transdermal therapeutic system is essentially a multilaminate structure that is composed of following constituents:

1. Drug: Drug is in direct contact with release liner. Ex: Nicotine, Methotrexate and Estrogens
2. Liners: Protects the patch during storage. Ex: polyester film.
3. Adhesive: Serves to adhere the patch to the skin for systemic delivery of drug. Ex: Acrylates, Polyisobutylene, Silicones.
4. Permeation enhancers: Controls the Release of the drug. Ex: Terpenes, Terpenoids, Pyrrolidones.
5. Solvents like alcohol, Ethanol, Methanol.
6. Surfactants like Sodium Lauryl sulphate, Pluronic F127, Pluronic F68.
7. Backing layer: Protect patch from outer environment. Ex: Cellulose derivatives, poly vinyl alcohol, Polypropylene Silicon rubber.

**TYPES OF TRANSDERMAL PATCHES<sup>[2]</sup>****a) Single layer drug in adhesive**

In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and also responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

**b) Multi -layer drug in adhesive**

This type is also similar to the single layer but it contains a immediate drug release layer and other layer will be a controlled release along with the adhesive layer. The adhesive layer is responsible for the releasing of the drug. This patch also has a temporary liner-layer and a permanent backing.

**c) Reservoir system**

In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or non porous. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymeric membrane which is compatible with drug.

**d) Matrix system**

The matrix system has a drug layer of a semisolid matrix containing drug solution or suspension. The adhesive layer in this patch surrounds the drug layer partially overlaying it. This is also known as monolithic device.

**e) Micro reservoir system**

In this type the drug delivery system is a combination of reservoir and matrix system. The drug reservoir is formed by suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogenously in a lipophillic polymer to form thousands of unreachable, microscopic spheres of drug reservoirs. This thermodynamically unstable dispersion is stabilized quickly by immediately cross linking the polymer in situ by using cross linking agents.

**f) Vapour patch**

In this type of patch the role of adhesive layer not only serves to adhere the various layers together but also serves as release vapour. The vapour patches are new to the market, commonly used for releasing of essential oils in decongestion. Various other types of vapor patches are also available in the market which are used to improve the quality of sleep and reduces the cigarette smoking conditions.

**RECENT TECHNIQUES FOR ENHANCING TDDS<sup>[3]</sup>****Structure-Based Enhancement Techniques*****Micro-fabricated Micro-needles***

Micro-fabricated micro-needles are devices which are hybrids of the hypodermic needle and transdermal patch through the use of microscopic needles that can deliver the drug effectively (like a hypodermic needle). Their small size offers the potential advantages of delivering large molecules across the stratum corneum without extreme pain to the patients.

***Macroflux***

These are devices having an area of around 8cm as well as 300 micro projections per 2cm with the length of individual micro projection less than 200µm. Three types of Macroflux have been designed. They include, Dry-Coated Macrofluxsystem-this is used for short period delivery that consists microprojection array coated with medicament that adhered to a elastic polymer adhesive backing. D-TRANS Macroflux system-this is also for short duration administration that consists of a microprojection array combined with reservoir of drug. E-TRANS Macroflux system-this is for on demand delivery that involves a microprojection array combined with an electro transport system.

***Metered-Dose Transdermal Spray (MDTS)***

Metered-dose transdermal spray (MDTSTM), originally developed at the Victorian College of Pharmacy [Monash University (Parkville Campus), Parkville, Victoria, Australia] and currently being commercialized by Acrux Limited [Melbourne, Victoria, Australia] has the potential to expand the growth of TDD systems by broadening patient acceptance and pharmaceutical applications for enhanced TDD. It is a liquid preparation in the form of solution that are used topically which is made up of a vehicle that is volatile cum non volatile in nature, which consists the completely dissolved medicament in solution. MDTS delivers a drug to the surface of the skin which is absorbed into the circulation on a sustained basis. The drug is delivered by a device placed gently against the skin and triggered, causing it to

release a light spray containing a proprietary formulation of the drug that quickly dries on the skin to form an invisible drug depot. As it would be from a patch, the drug is then absorbed steadily for a predetermined amount of time.

The MDTs has the following potential advantages:

- ☐ It improves delivery potential without skin irritation due to its non-occlusive nature.
- ☐ Increased acceptability.
- ☐ Dose flexibility
- ☐ Simple manufacture.

### **Electrically-Based Enhancement Techniques**

#### ***Iontophoresis***

Iontophoresis may be defined as the facilitation of ionizable drug permeation across the skin by an applied electrical potential, the driving force of which may be simply visualized as electrostatic repulsion. A typical iontophoresis device consists of a battery, microprocessor controller, drug reservoir and electrodes. The technique involves the application of a small electric current (usually 0.5 mA/cm<sup>2</sup>) to a drug reservoir on the skin, with the similarly charged electrodes (on the surface of the skin) placed together in the drug reservoir producing a repulsion effect that effectively drives the solute molecules away from the electrode and into the skin

#### ***Acoustical Methods***

Ultrasonic waves, as well as short-duration shock waves, have been used to facilitate transdermal delivery. Ultrasound at various frequencies in the range of 20 kHz-16MHz has been used to enhance skin permeability by a method called sonophoresis. Traditionally, ultrasound at high frequencies ( $f > 1$  MHz, therapeutic ultrasound) was a popular choice for sonophoresis. However, transdermal transport enhancement induced by low-frequency ultrasound ( $f < 100$  kHz) is significantly greater than that induced by therapeutic ultrasound. Accordingly, low-frequency sonophoresis has received particular attention during the past decade. In addition to heating, ultrasound is also known to generate cavitation, which is the formation, oscillation and, in some cases, collapse of bubbles in an ultrasonic pressure field. Cavitation is only generated under specific conditions (e.g., low-frequency ultrasound) that differ from those of ultrasonic heating or imaging devices. The opportunity for transdermal drug delivery is that cavitation bubbles concentrate the energy of ultrasound and thereby enable targeted effects at the site of bubble activity. Because bubbles are more difficult to

grow and oscillate within densely-packed tissue, cavitation preferentially occurs within the coupling medium (e.g., a hydrogel) between the ultrasound transducer and skin.

### ***Photomechanical Waves***

Photomechanical waves (PW's) are the pressure pulses produced by ablation of a material target (polystyrene) by Q-switched or mode-locked lasers. Photomechanical waves are able to render the stratum corneum more permeable to macromolecules via a possible transient permeabilisation effect due to the formation of transient channels. The largest molecule that has been reported to be delivered through the rat skin to date has a molecular weight of 40,000Da. Suggestions have been made that many clinically important proteins such as insulin (6000 Da) and hematoprotien (48000 Da) are within or close to the delivery capability range of PW's. However; this relatively new technique does not yet seem to have produced any human clinical data.

### ***Electroporation***

In this method, short and high-voltage electrical pulses are applied to the skin thus the diffusion of drug is improved with the increasing permeability. The electrical pulses are considered to form small pores in the stratum cornea, through which transportation of drug occurs. For the safe and painless administration, the electrical pulses introduced by closely spaced electrodes to reserved the electric field within the stratum cornea.

### ***Electro-osmosis***

If a charged porous membrane is subjected to a voltage difference, a bulk fluid or volume flow, called electro osmosis occurs without concentration gradients, suggesting that this flow is not diffusion. This bulk fluid flow by electro osmosis was found to be of the order of micro liters per hour per square centimeter of hairless mouse skin. The electro-osmotic flow occurs from anode to cathode, thus enhancing the flux of positively charged (cationic) drugs and making it possible to deliver neutral drugs.

### ***Chemical enhancers***

Chemical enhancers can increase skin permeability by various mechanisms, including enhancing solubility, partitioning the stratum corneum, fluidizing the crystalline structure of the stratum cornuem and causing dissolution of stratum cornuem lipids.



## Velocity Based Enhancement Techniques

### *Needle-Free Injections*

The highest value, least developed and most technically challenging group of needle-free technologies is prefilled, disposable injectors. The development of such technologies is primarily driven by the demand for a convenient, non-invasive alternative to the conventional needle and syringe injection. The earliest needle free injectors became available as early as 1866, when the French company H. Galante manufactured an “Apparatus for aqua puncture”. Some of the needle free injectors under development are:

□ **Intraject:**

Intraject system is the world’s first disposable, needle free injection device for the delivery of liquid medicaments. Intraject is specially designed to meet the patient needs; being pre-filled and disposable the system is designed for unobtrusive, contamination free self injection. Intraject offers pharmaceutical companies opportunity to extend the product lifestyle and manage patent expiry.<sup>[14]</sup>

□ **Implaject:** Simple, hand-held needle free injection device. Can be configured to be reusable with disposable cartridges.<sup>[13]</sup>

□ **Jet Syringe:** A jet injector is a type of medical injecting syringe that uses a high-pressure narrow jet of the injection liquid instead of a hypodermic needle to penetrate the epidermis. It is powered by compressed air or gas, either by a pressure hose from a large cylinder, or from a built-in gas cartridge or small cylinder. Jet injectors are used for mass vaccination, and as an alternative to needle syringes for diabetics to inject insulin.<sup>[15]</sup>

□ **Iject:** Iject is a small, lightweight, gas-powered injection system designed for home or professional use. This system has two versions, one is a pre-filled, single-use disposable injector, and the other is a reusable injector that accepts pre-filled medication cartridges.<sup>[13]</sup>

□ **Mini-ject:** The Mini-Ject can deliver a wide range of drugs, ranging from small molecules to large proteins, fragile antibodies, and vaccines. Delivery can be targeted to intradermal, subcutaneous or intramuscular depending on the clinical need. No other single-use needle-free delivery technology provides the same level of performance as the Mini-Ject technology with the ability to target specific tissue layers over such a broad range of drug volumes (0.1 mL to 1.3 mL) and viscosities.<sup>[13]</sup>



***Powderject Device***

The solid drug particles are propelled across the skin with the aid of high-speed gas flow. This consists of a gas canister that allows helium gas at high pressure to enter a chamber at the end of which is a drug cassette containing powdered drug between two polycarbonate membranes. After release, the instantaneous rupture of both membranes results in the gas to expand quickly which forms a strong motion like a wave that travels down the nozzle. This takes place at the speed of 600-900 m/s.

**Other Enhancement Techniques*****Transfersomes***

This device penetrates the skin barrier along the skin moisture gradient. Transfersome carriers can create a drug depot in the systemic circulation that is having a high concentration of drug. Transfersomes contain a component that destabilizes the lipid bilayers and thus leading to the deformable vesicles.

***Medicated Tattoos***

Med-Tats are a modification of temporary tattoo which contains an active drug substance for transdermal delivery. This technique is useful in the administration of drug in those children who are not able to take traditional dosage forms.

***Skin Abrasion***

This involves direct removal or disruption of the upper layers of the skin to provide better permeation of topically applied drug substance. In general, one approach is adopted to create micro channels in the skin by eroding the impermeable outer layers with sharp microscopic metal granules are generally known as Micro-scissuining. It facilitates the transfer of drug substance to the blood circulation by applying heat to the skin that increases the temperature and ultimately led to increase in microcirculation and permeability in blood vessel. CHADD (Controlled Heat Assisted Drug Delivery) system consists of a small unit that is used for heating purpose, placed on top of a conventional patch device. An oxidation reaction occurs within the units which tend to form heat of limited intensity and duration.

**Laser Radiation**

This involves the exposure of the skin to the laser beam that results in the ablation of the stratum cornea without damaging the epidermis which remains in contact with it. Removal of the stratum cornea by this technique is considered to improve the delivery of lipophilic and hydrophilic drugs.

**Magnetophoresis:** The effect of magnetic field on diffusion flux of drug substance was found to be enhance with increasing applied strength.

**Table1: Marketed Products of Modified Transdermal Drug Delivery System<sup>[1]</sup>**

Brand Name	Company Name	Enhancement Technique	Drug product available
<b>Macroflux</b>	Alza Corporation	Microprojection	Vaccines and Therapeutic proteins
<b>E-Trans</b>	Alza Corporation	Iontophoresis	Fentanyl
<b>SonoPrep</b>	Sontra Medical Corporation	Ultrasound	Peptides and Other large molecules
<b>SonoDerm</b>	Imarx	Ultrasound	Large molecules (Insulin)
<b>Intraject</b>	Weston Medical	Needleless injectors	Vaccines
<b>Powderject</b>	Powderject Pharmaceutical	Needleless injectors	Insulin
<b>Med-Tat</b>	Lipper-Man Ltd.	Medicated Tattoos	Acetaminophen, Vitamin C
<b>CHADD</b>	Zars, Inc	Heat	S-Caine (Lidocaine and Tetracaine)

**Table: 2 List of Marketed Transdermal Products of Various Drugs(Global)<sup>[1]</sup>**

TRADE NAME	DRUG	INDICATION	MANUFACTURER
Transderm-ScopR	Scopolamine	Motion sickness	Alza/Norvatis
1.Nitrodisc 2. Deponit 3. Nitrodur 4. Minitran 5.Transderm-NitroR	Nitroglycerine	Angina pectoris	1.Roberts Pharmaceuticals 2. Schwarz-Pharma 3. Key Pharmaceuticals 4.3M Pharmaceuticals 5. Alza/Norvatis
Catapres TTSR	Clonidine	Hypertension	Alza

1.FemPatch 2.Climaderm 3.Alora 4. Estraderm 5. Climara	Estradiol	<b>Postmenstrual syndrome</b>	1. Parke-Davis 2.Ethical.Holdings/Wyeth-Ayerest 3.TheraTech/ Proctol and Gamble 4. Alza/Norvatis 5.3M Pharmaceuticals /Berlex Labs
1.Nuvelle TS 2.Fematrix	Estrogens /Progesterone	<b>Hormone replacement therapy Postmenstrual syndrome</b>	1.Ethical Holdings/Schering 2.Ethical Holdings/ Solvay Healthcare Ltd
<b>DuragesicR</b>	Fentanyl	<b>Chronic pain</b>	<b>Alza/Janssen Pharmaceutical</b>
1.Prostep 2.NicotinellR 3.NicodermR	Nicotine	<b>Smoking cessation</b>	1.Elan Corp./Lederle Labs 2. Novartis 3. Alza/GlaxoSmithKline
1.Testoderm TTSR 2.Androderm	Testosterone	<b>Testosterone deficiency</b>	1. Alza 2.TheraTech/GlaxoSmithKline
<b>Ionsys</b>	Fentanyl HCL(Iontophoresis)	<b>Acute post operative pain</b>	<b>Alza, Mountain View, CA</b>
<b>NuPatch 100</b>	Diclofenac diethylamine	<b>Anti Inflammatory</b>	<b>Zydus Cadila</b>
<b>Oxytrol</b>	Oxybutynin	<b>Overactive bladder</b>	<b>Watson Pharma (Corona, CA)</b>
<b>Neupro</b>	Rotigotine	<b>Parkinson's disease</b>	<b>Schwarz Pharma (Mequon, WI)</b>
<b>Exelon</b>	Rivastigmine	<b>Dementia</b>	<b>Novartis (East Hannover, NJ)</b>
<b>Emsam</b>	Selegiline	<b>Major depressive disorder</b>	<b>Bristol-Myers Squibb (Princeton, NJ)</b>
<b>SonoPrep</b>	Lidocaine(Ultrasound)	<b>Local dermal anaesthesia</b>	<b>Echo Therapeutics (Franklin, MA)</b>

Table: 3 List of Marketed Products Available In India

TRADE NAME	DRUG	INDICATION	MANUFACTURER
ETS Patch <sup>TM</sup>	Estradiol	Hormone replacement therapy	Emcure
Exelon <sup>TM</sup>	Rivastigmine	Dementia	Novartis
Proxym patch <sup>TM</sup>	Piroxicam	NSAID	Emcure
Nupatch <sup>TM</sup>	Diclofenac	Anti-inflammatory	Zydus Cadila
Fen-touch <sup>[TM]</sup>	Fentanyl	Chronic pain	Sparsh pharma
Diclo-touch <sup>TM</sup>	Diclofenac	Anti-inflammatory	Sparsh pharma
Artho-touch <sup>TM</sup>	Ketoprofen	Tennis-elbow, Arthritis	Sparsh pharma
Memory-touch <sup>TM</sup>	Rivastigmine	Dementia	Sparsh pharma

Nitroderm TTS™	Nitroglycerine	Angina Pectoris	Novartis
Ketopatch™	Ketoprofen	Arthritis	Emcure

### 1.) ETS patch<sup>[5]</sup>

MRP: 49 Rs.

1.8mg of estradiol per patch

MANUFACTURED BY: EMCURE Pharmaceuticals

### INDICATION

Carcinoma prostate, Contraceptive use, Dysmenorrhoea, Functional uterine bleeding, Menopausal syndrome, Vaginitis.

### PRECAUTION

Breast cancer, Cardiovascular disease, jaundice, Endometrial cancer, Hepatic impairment, Lactation, Liver damage, Migraine, Pregnancy, Undiagnosed vaginal bleeding, gall bladder diseases, dementia.

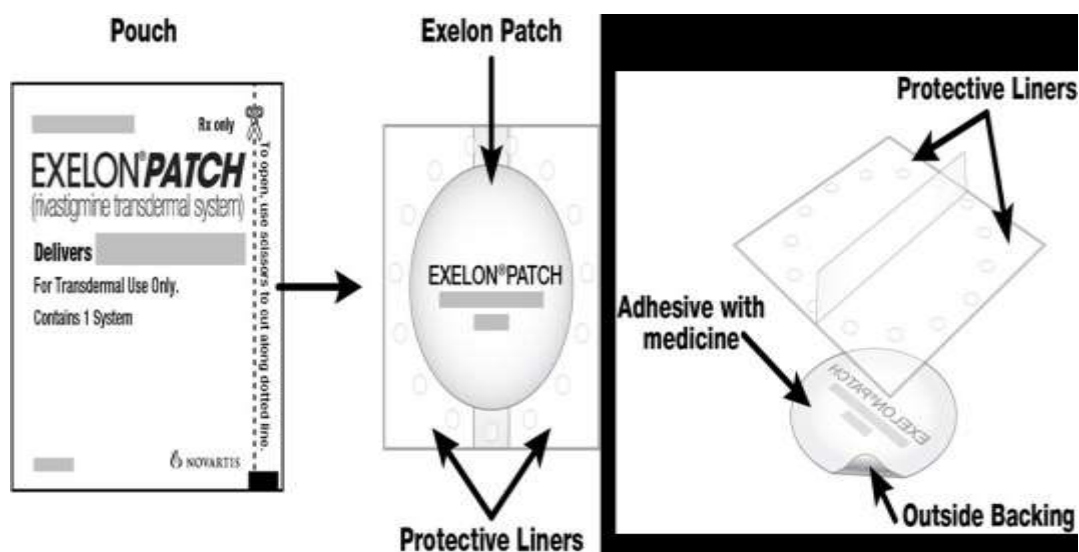
### 2.) EXELON PATCH<sup>[12]</sup>

13.3mg of rivastigmine per patch

MANUFACTURED BY: NOVARTIS

INDICATION: Alzheimer's disease, Dementia

PRECAUTION: Asthma, Peptic ulcer, hypersensitivity



### 3.) PROXYM PATCH<sup>[7]</sup>

MRP: 49Rs

48mg of piroxicam per patch

MANUFACTURED BY: EMCURE

INDICATION: Rheumatic disorders, Acute gout, Acute musculoskeletal conditions, Postoperative pain, Juvenile idiopathic arthritis.

PRECAUTION: Hypersensitivity, Active peptic ulceration, Pregnancy (3rd trimester) and lactation.

### 4.) Nupatch<sup>[6]</sup>

MRP: 37Rs

100mg of Diclofenac per patch

MANUFACTURED BY: ZYDUS CADILA

INDICATION: Low backache, Muscle spasm, Myalgia, Sprains

PRECAUTION: Avoid contact with eyes



5.) Fen-touch<sup>[8]</sup>**MANUFACTURED BY: SPARSH PHARMA**

Strength	Fentanyl per patch	Patch Size
12.5 mcg/hr	1.25 mg	5cm <sup>2</sup>
25 mcg/hr	2.5 mg	10cm <sup>2</sup>
50 mcg/hr	5.0 mg	20cm <sup>2</sup>
75 mcg/hr	7.5 mg	30cm <sup>2</sup>
100 mcg/hr	10.0 mg	40cm <sup>2</sup>

**FEN-TOUCH<sup>TM</sup>** is licensed to Dr.Reddy's Laboratories Ltd. for the Indian market under the brand name FINRID.

**Precautions**

- Application site is preferably void of hair, and must be clean and dry. Wash the site before applying patch
- Do not apply to damaged areas (irritated, injured, cut area of the skin)
- Do not apply where cosmetics such as cream, lotion, gel etc., are already applied
- Do not apply if patch is damaged, opened or peeling must be applied only one time. It should not be removed/re-applied; adhesive stickiness is reduced when the patch is re-applied
- After removal of a previous patch, the next patch should be applied to a different skin site should not be applied when the patient has a fever, because the high body temperature will cause an increased rate of Fentanyl delivery.

Fentanyl should be avoided:

- In patients with acute or severe bronchial asthma.
- In the management of intermittent pain.
- For patients who are not opioid tolerant.
- The management of acute or mild pain.



6.) Diclo-touch<sup>[TM]</sup> [11]

**MANUFACTURED BY: SPARSH PHARMA**

**USED FOR:**

- Tennis Elbow
- Arthritis
- Scapula Inflammation
- Tendon Tenovaginitis
- Peritendinitis
- Swelling,
- pain after Trauma
- Myalgia

### **PRECAUTIONS**

- Apply patch immediately after taking out from the pouch
- Close the pouch after removal of the patch
- Protect from light
- Keep out of reach of children
- Apply patch to non hairy part on the body
- Apply patch once a day.





7.) Artho-touch<sup>[TM]</sup> [10][4]

**MANUFACTURED BY: SPARSH PHARMA**

**USED FOR:**

- Tennis Elbow
- Deformans Arthritis
- Scapula Inflammation
- Tendon Tenovaginitis
- Peritendinitis
- Swelling, Pain after Trauma



8.) MEMORY-TOUCH<sup>[TM]</sup> [9]

**MANUFACTURED BY: SPARSH PHARMA**

Indication: For the treatment of patients with mild to moderately severe dementia of the Alzheimer type and dementia associated with Parkinson's disease.

**RIVASTIGMINE TRANSDERMAL PATCH DRUG DELIVERY RATE**

MEMORY-TOUCH 9mg 4.6mg / 24 hr.

MEMORY-TOUCH 18mg 9.5mg / 24 hr.

**CONCLUSION**

This article provides valuable information regarding the transdermal drug delivery systems. The foregoing shows that TDDS have great potentials, being able to use for both hydrophobic and hydrophilic active substance into promising deliverable drugs. To optimize this drug delivery system, greater understanding of the different mechanisms of biological interactions, and polymer are required. TDDS is a realistic practical application as the next generation of drug delivery system.

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