ISSN: 2279 - 0594

Available Online at www.jbpr.in

Journal of Biomedical and Pharmaceutical Research 3 (3) 2014, 88-101

REVIEW ARTICLE

A REVIEW ON THE RECENT INNOVATIONS IN TRANSDERMAL DRUG DELIVERY FOR HERBAL THERAPY

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Received 07 June 2014; Accepted 20 June 2014

ABSTRACT

This review focuses on the recent innovation in Transdermal drug delivery system which can be a stand for the research and development of pharmaceutical dosage form for transdermal drug delivery. TDDS (transdermal drug delivery system) improve beneficial value and drug safety by further site definite the way and temporal position in the body's vital to reduce the number and size of doses necessary to achieve the objective of systemic medication through topical application to the intact skin surface. TDDS has abundant advantages more than usual drug delivery route. Transdermal route or therapy is non-invasive that includes lack of first pass metabolism effect, high bioavailability and steady drug plasma concentration. A Transdermal Patch is an adhesive patch that has a coating of medicine (drug) that is placed on the skin to deliver specific dose of the medicine (drug) into the bloodstream over a period of time. The present review focused on the delivery of some herbal agents through transdermal route. The main principle of developing unconventional drug delivery technologies is to offer more convenience for patients and increase the effectiveness and protection of drug. The aim of the present review at formulation of transdermal patches incorporating herbal drug components. Transdermal patch is a medicated adhesive pad that is designed to release the active ingredient at a constant rate over a period of several hours to days after application to the skin. It has been found that drugs from herbal origin can be utilized with enhanced efficacy by incorporating in transdermal drug patches. Herbal transdermal patches which aids to quit smoking, relieve stress, increase sexuality, insect repellant patches, detoxification, male energizer, postpone menopause are available. The objective and aim of the transdermal drug delivery system is topically administered drug in the form of patches that is delivering the drug in the body through the skin for systemic effect at a predetermined time period.

Key words: Transdermal Patch, Herbal Therapy, Polymers, Medicine.

INTRODUCTION:

Nowadays about 74% of drugs are taken orally and are found not to be as valuable as most wanted. To advance such characters transdermal drug delivery system was emerged. With the creation of current time of pharmaceutical dosage forms, transdermal drug delivery system (TDDS) recognized itself as an important part of novel drug delivery systems. Transdermal dosage forms, still a costly alternative to conventional formulations, are becoming popular because of their exclusive advantages. Improved bioavailability, Controlled absorption, extra uniform plasma levels, painless and reduced side effects easy application and flexibility of terminating drug administration by simply removing the patch to the skin are some of the potential advantages of transdermal drug delivery [1]. Oral Conventional dosage forms like tablets and capsules are most widely used drug delivery system but both dosage forms face problem of gastric drug/enzyme instability first pass metabolism. Oral route has many further problems like unpleasant taste, odour and color. Numerous additional problems are arising during taking pills; hence problems are being faced during treatment. Sometimes Patients become non-compliant. TDDS patches drugs are used by continuous release so they show their effect for exact duration and Transdermal patch is non-irritating and noninvasive technique. It is attractive alternative techniques over conservative techniques for systemic administration of drug [2]**.** Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from usual topical drug delivery [3]. With the purpose of deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical and physicochemical

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properties of the skin are to be considered. Delivery of drug via transdermal provides the most important edge over oral and injectables routes by avoiding first pass metabolism and increasing patient compliance respectively [4]. During the last decade transdermal drug delivery system has gained a lot of interest as it offers many advantages over the conventional dosage forms and oral controlled release delivery systems especially less frequency of administration, avoidance of hepatic first pass effect, reduction in gastrointestinal side effect and improves patient compliance [5]. Transdermal drug delivery systems are defined as self-contained, discrete dosage forms which, when applied to intact skin, deliver the drug, through the skin, at a controlled rate to systemic circulation. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation, which often causes undesirable side effects Thus various forms of Novel drug delivery system such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems etc. emerged [6].

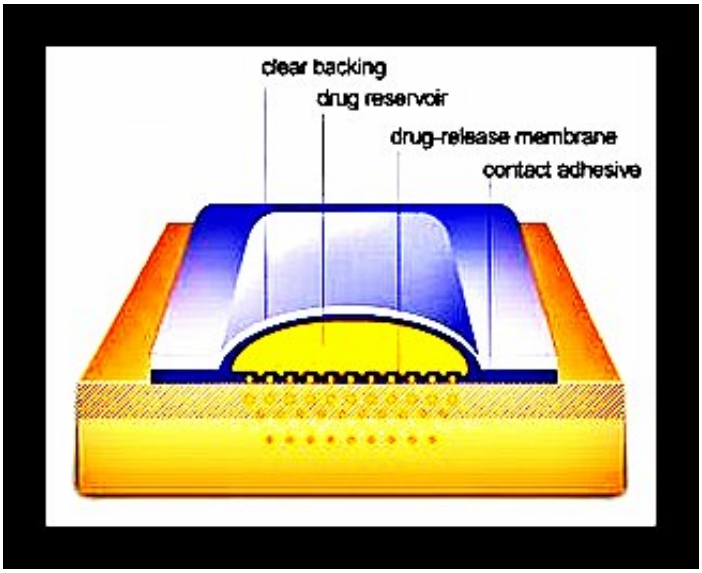

Figure 1: Various Parts of TDDS

TRANSDERMAL PATCH: [7, 8, 9, 10]

A **transdermal patch** is defined as adhesive medicated patch that is placed on to the above skin to deliver an exact dose of drug through the skin into the bloodstream with a predetermined rate of release to reach in the body. Today the most common transdermal system present in the market mainly based on semi permeable membranes which were called as **patches. Transdermal drug delivery systems** (TDDS), also known as **"Transdermal patches"** or **"Skin patches"** are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin and in the bloodstream**.**

MAIN INGREDIENTS USED FOR THE PREPARATION OF TRANSDERMAL DRUG DELIVERY SYSTEM [11, 12]

1.Liners- It provides the protection of patches during storage and the liner should be removed previous to use.

2.Adhesive- It served to adhere the components of the patch together along with adhering the patch to skin.

3.Membrane- Its controls the drug releases from the multi layer patches. It's also known as the permeation enhancer.

4.Drug- Drug reservoir is direct contact with release liner.

5.Backing- protects the patches from outer environment.

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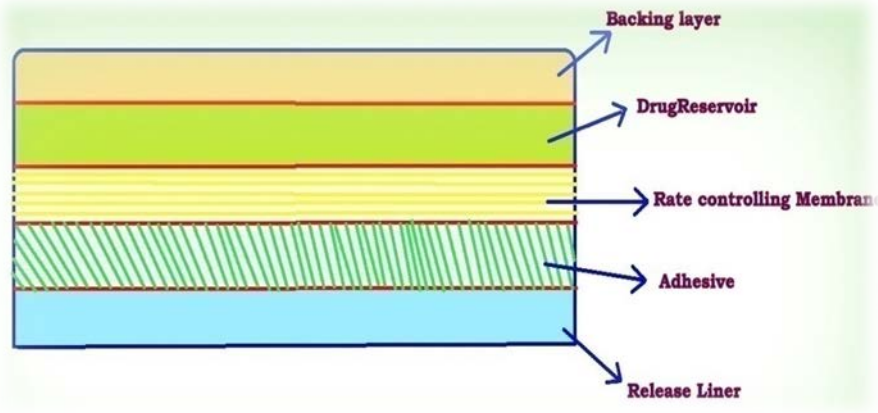
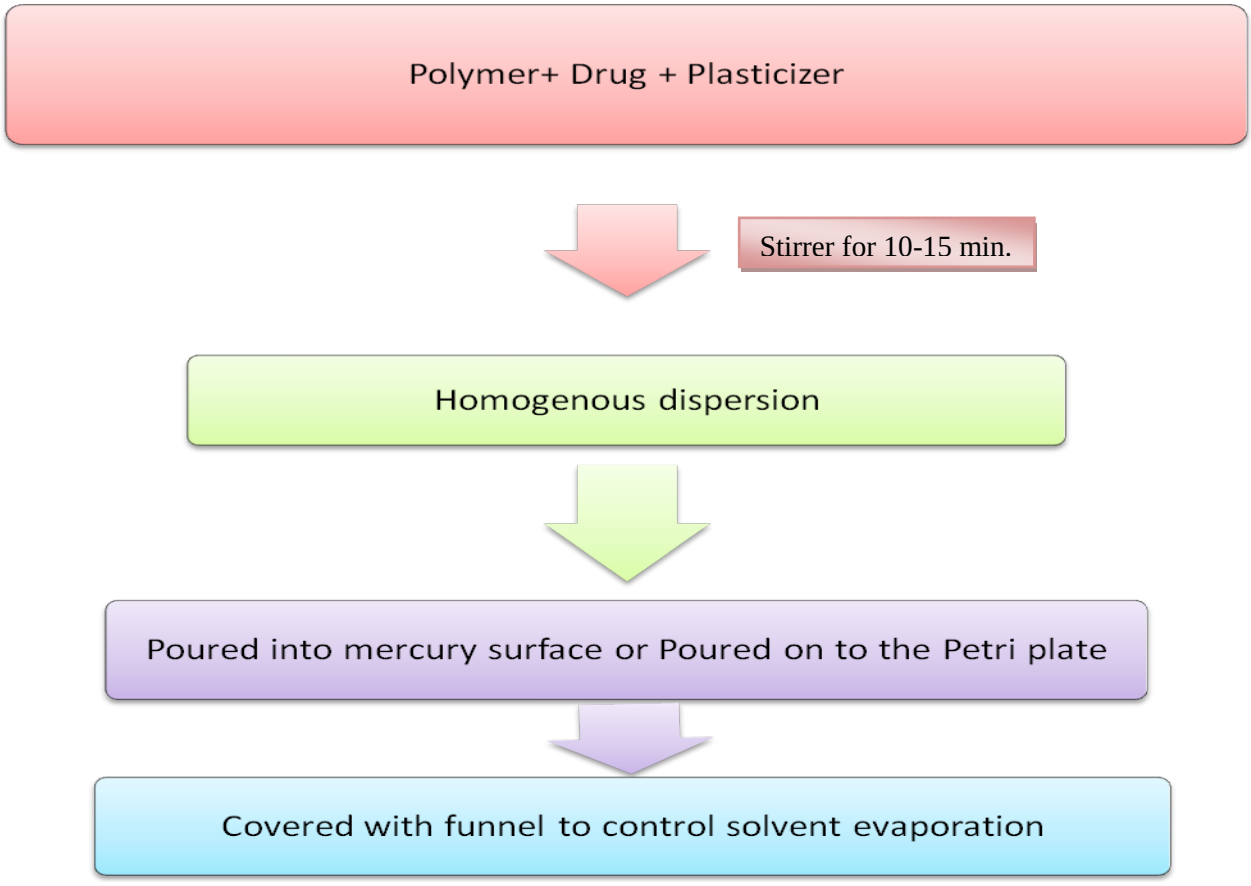


Figure 2: Different layers of transdermal patches

METHOD OF PREPARING TRANSDERMAL PATCHES: [13, 14, 15,]

Method of preparation of TDDS was summarized by modifying the earlier reported methods. The patches were prepared by solvent casting method. The polymer (for example PVP/HPMC) was taken in a beaker with a minimum quantity of the solvent. Then 2/3rd of the solvent was mixed with the other polymers (for example PVA) and was added firstly with stirring at lower rpm and later at a higher speed. The plasticizer was added and homogeneously mixed and the drug was included with enduring agitation and the volume was made up. The films were cast onto a suitably designed and fabricated glass mould and then dried in oven at 40°C. The films were removed by using sharp blade by inserting along the edges of the film. The dried films were wrapped in butter paper and stored in a closed container away from light and in cool place.



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TYPES OF TRANSDERMAL PATHCES: [16, 17, 18, 19]

1. Single layer drug-in-Adhesive Patches: In this system, the drug is remains in contact with the adhesive layer which is attached to the skin. In the layer of adhesive helps to releasing the drug and also serve to adhere to the various layers together along with the skin.

Figure 3: Single layer drug in adhesive type's transdermal patches.

2. Multi-layer drug-in-Adhesive Patches: The multi layer drug in adhesive is similar to the single layer drug in adhesive which involves the drug introduction directly into the adhesive layer. In this system one of the layers is immediate to release the drug from the reservoir. This patch also has a permanent backing and temporary liner-layer.

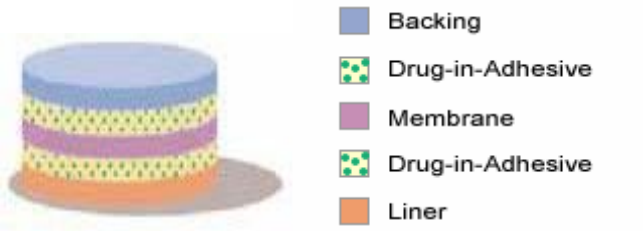

Figure 4: multiple layer drug in adhesive type transdermal patches.

3. Reservoir type patches: The reservoir transdermal system has a separate drug layer unlike the single layer drug-in-adhesive and multilayer-drug-in-adhesive system. In this system, it includes a compartment for liquid that contains a solution or suspension of drugs separated from the liner by a membrane and adhesive. This patch system is also backed by the backing layer. In the reservoir system the rate of release is zero order.

Figure 5: Reservoir type transdermal patches.

4. Matrix type patches: The matrix system consist a medicament layer of a semisolid matrix that contains a drug as a solution or suspension; that is direct contact with the liner layer. In this device the adhesive layer surrounds the drug layer partially overlaying it.

Figure 6: matrix type transdermal patches.

5. Vapour patches: In this type of patch system the adhesive layer not only serves to adhere the various layers together but also releases vapour. These patches are new to the market, and commonly used for releasing of essential oils for up to 6 hrs. These patches release of essential oils and are used in cases of decongestion mainly. Many types of vapour patches are available in the market which are used to improve the quantity of sleep and reduces the cigarette smoking condition.

ADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM: [20, 21, 22, 23]

Transdermal drug delivery systems offer several important advantages over more traditional approaches, including: It is safe, effective and may be withdrawn easily as per need of the patient.

Numerous considerable advantages of transdermal drug delivery (TDD) are limitation of hepatic first pass metabolism, enrichment of therapeutic efficiency and maintenance of steady plasma level of the drug. The major advantage of TDDS are given as follows-

- The hepatic first pass metabolism is avoided.
- Sustained and controlled delivery over a prolong period of time.
- Direct access to target or diseased site.
- Provide relatively steady and sustained drug concentration in plasma in contrast to conventional systems where peaks and troughs are a common feature.
- Provides utilization of drugs with short biological half lives.
- Ease of dose termination in any adverse reactions either systemic or local.
- Inter and intra patient variations.
- Termination of therapy is easy at any point of time.
- Variability due to factors such as pH intestinal motility, food intake, etc, which make vast difference in the bioavailability of the drugs given through oral route, are not existent.
- Painless and Suitable administration.
- Expected and unlimited duration of activity.
- A stable rate of absorption is possible in a huge variety of adverse patient population.

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- Improving physiological and pharmacological comeback.
- Maintain plasma concentration of potent drugs.
- Greater patient compliance due to exclusion of multiple dosing profiles.
- Ability to deliver drug more selectively to a particular site.
- Provide appropriateness for self administration.
- Avoidance of gastro intestinal incompatibility.
- Ease of dose termination in any adverse reactions either systemic or local.
- Drugs that cause gastro intestinal upset can be good candidates for Transdermal delivery because this method avoids direct effects on stomach and intestine.
- Avoiding the fluctuation in drug levels.
- At some stage in application of gel amount and area of application are not specify but in patch both are specific.
- Condensed side effects and improved therapy due to preservation of plasma levels up to the end of the dosing interval.
- Elasticity of terminating the drug administration by simply removing the patch from the skin.

DISADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM: [24, 25, 26, 27]

- Only relatively potent drugs are suitable candidates for TDDS.
- Local irritation and arrhythmia are possible. Enzymes in epidermis or derived from micro organisms present on the skin may denature the drugs.
- Can be used only for drugs, which require very small plasma concentrations for action.
- The drug must have some desirable physicochemical properties for penetration through stratum corneum.
- The barrier function of the skin changes from one site to another on the same person, from person to person and with age.
- Variation in absorption efficiency at different sites of skin.
- Difficulty of adhesion to certain skin types like excess oily skin.
- Difficulty in duration of time for which a patch can be left on any area due to permeability changes (usually not more than 7 to 10 days).
- The transdermal delivery will be very difficult, if the drug dose required is more than 10 mg/day for their therapeutic application.
- Another significant disadvantage of Transdermal drug delivery is that skin is less permeable because it serves as protective barrier for the entry of foreign particles.
- In order to maintain constant release states, transdermal patches must contain surplus of active drug.

LIMITATION OF TRANSDERMAL DRUG DELIVERY SYSTEM: [28, 29, 30]

- Limitation of TDDS can be overcome to some extent by novel approaches such as Iontophoresis, electroporation and ultrasound.
- Transdermal drug delivery system has limited skin permeability.
- Restricted to potent drug and Significant lag time.
- A molecular weight less than 500 Dalton (Cannot use for large molecules) is essential to ensure ease of diffusion across the SC, since solute diffusivity is inversely related to its size.
- Pre systemic metabolism the presence of enzymes in the skin such as peptidases might metabolise drug in inactive form and reduce efficacy of drug.
- Skin irritation and sensitization; referred to as Achilles heel of dermal and transdermal delivery.
- Transdermal delivery is neither practical nor affordable when required to deliver large doses of drugs through skin.
- Drug of drug formulation may cause irritation or sensitization.
- Not practical, when the drug is extensively metabolized in the skin and when molecular size is great enough to prevent the molecules from diffusing through the skin.
- Not suitable for a drug, which doesn't possess a favourable, o/w partition coefficient.
- The drug must have some desirable physicochemical properties for penetration through stratum corneum and if the drug dose required for therapeutic value is more than 10 mg/day, the transdermal delivery will be very difficult.
- Only relatively potent drugs are suitable candidates for Transdermal drug delivery system because of the natural limits of drug entry imposed by the skin is impermeability.
- Some patients develop contact dermatitis at the site of application for one or more of the system components, necessitating discontinuation.
- Clinical need is another area that has to be examined carefully before a decision is made to develop a transdermal product.

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- The barrier function of the skin changes from one site to another on the same person, from person to person and with age.
- TDDS cannot deliver ionic drugs.
- TDDS cannot achieve high drug levels in blood/plasma.
- TDDS cannot deliver drugs in a pulsatile fashion.
- TDDS cannot develop if drug or formulation causes irritation to skin.

IDEAL PROPERTIES OF TRANSDERMAL DRUG DELIVERY SYSTEM: [2, 6]

- Shelf life up to 2 years
- Small size patch (i.e., less than 40 cm^2)
- Convenient dose frequency (i.e., once a day to once a week)
- Cosmetically acceptable (i.e., clear, white colour)
- Simple packaging (i.e., minimum number of pouches and steps required to apply the system)
- Easy removal of the release liner (i.e., for children and elderly patients)
- adequate skin adhesion (i.e., no fall off during the dosing interval and easy removal without skin trauma)
- No residue i.e., —cold flow (around the edge of the patch in storage or after application to skin or beneath the patch after removal)

MECHANISM OF ACTION OF TRANSDERMAL PATCHES: [31]

The function of the transdermal patch and the flow of the active drug ingredient from the patch to the circulatory system via skin transpire through different methods. For a systemically active drug to reach a target tissue, it has to take some physicochemical properties which make easy the sorption of the drug through the skin and enter the microcirculation.

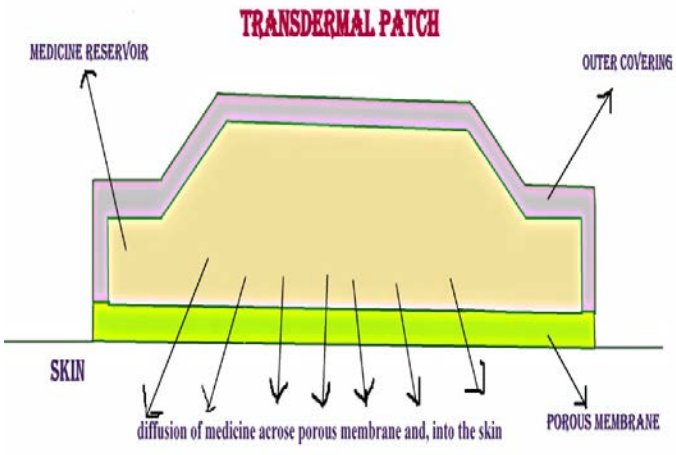

Figure 7: Showing the Mechanism of Drug release from Transdermal Patch

MODERN TECHNIQUES OF TRANSDERMAL DRUG DELIVERY SYSTEM: [32, 33, 34, 35, 36, 37, 38]

- **IONTOPHORESIS:** It involves passing of current (few milli amperes) to skin limited to a certain area using the electrode remains in contact with the formulation which is to be administered. Pilocarpine delivery can be taken as example to induce sweat in the diagnosis of cystic fibrosis and Iontophoretic delivery of lidocaine is considered to be a nice approach for rapid onset of anesthesia.
- **ELECTROPORATION:** Electroporation involves the application of high- voltage pulses to induce skin perturbation. High voltages (≥100 V) and short treatment durations (milliseconds) are most frequently employed. The increase in skin permeability is suggested to be caused by the generation of transient pores during electro poration. The technology has been successfully used to enhance the skin permeability of molecules with differing lipophilicity and size (i.e., small molecules, proteins, Peptides, oligo nucleotides).
- **MAGNETOPHORESIS:** This method involves the application of a magnetic field which acts as an external driving force to enhance the diffusion of a diamagnetic solute across the skin. Skin exposure to a magnetic field might also induce structural alterations that could contribute to an increase in permeability. In vitro studies showed a magnetically induced enhancement in benzoic acid flux, which was observed to increase with the strength of the applied magnetic field. The effect of magnetic field on diffusion flux of drug substance was found to enhance with increasing applied strength.
- **ULTRASOUNDS:** In these techniques, there is a mixing of drug substance with a coupling agent (usually with gel, cream or ointment) that causes ultrasonic energy transfer from the system to the skin. This involves rupturing the lipids present in stratum cornea, which allows the medicament to permeate via biological barrier.
- **MICROSCISSUINING:** It is a process which creates micro channels in the skin by eroding the impermeable outer layers with sharp microscopic metal granules.
- **MICROPORATION:** Microporation involves the use of micro needles that are applied to the skin so that they pierce only the stratum corneum and increase skin permeability. Microneedles are needles that are 10 to 200 µm in height and 10 to 50 µm in width. Microneedles do not stimulate the nerves, so the patient does not experience pain or discomfort. They are usually drug

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coated projections of solid silicon or hollow, drug filled metal needles.

- **SKIN ABRASION:** In this technique, the upper layers of the skin is directly removed or disrupted, so that it easily helps in permeation of topically applied medicaments. There are also some devices that are based on techniques which are employed by dermatologists for superficial skin resurfacing (e.g. micro dermabrasion) that have use in the treatment of acne, scars, hyper pigmentation and other skin blemishes.
- **NEEDLE-LESS INJECTION:** In this transdermal delivery system, the liquid or solid particles are fired at supersonic speeds through the outer layers of the skin using a reliable energy source for delivering the drug. The mechanism is basically, forcing compressed gas (helium) via a nozzle, such that the resultant drug particles entrained within the jet flow that travels at sufficient velocity for skin penetration.
- **MICRONEEDLES:** Microneedles developed as a means to deliver drugs into the skin by invasive manner. Solid micro needles have been shown to painlessly pierce the skin to increase skin permeability to a variety of small molecules, nanoparticles sand proteins from an extended-release Patch. Microneedles have been dip coated with a variety of compounds such as small molecules, DNA, proteins, and virus particles. In a recent study, naltrex one was administered to healthy volunteers whose skin was pre-treated with micro needles. After applying the naltrex one patch, therapeutic levels of naltrex one achieved.
- **ELECTRO-OSMOSIS:** To the porous membrane which is having some charge, a voltage difference is applied to it, thus a bulk fluid or volume flow takes place with no concentration gradients. This process is known as electro-osmosis.
- **LASER RADIATION:** This method involves direct and controlled exposure of a laser to the skin which results in the ablation of the stratum corneum without significantly damaging the underlying epidermis. Removal of the stratum corneum using this method has been shown to enhance the delivery of lipophilic and hydrophilic drugs. Photomechanical waves significantly led to the stratum cornea highly permeable to drug substance through a possible permeabilisation mechanism due to development of transient channels.
- **THERMOPHORESIS:** The skin surface temperature is usually maintained at 32°C tetracaine and fentanyl from transdermal patches with attached heating devices was shown to increase as a result of the elevated temperature at the site of delivery. However, the effect of temperature on the delivery of penetrates greater than 500 Daltons has not been reported.

BENEFICIAL USE OF HERBAL TRANSDERMAL THERAPY: [39, 40, 41, 42, 43]

There are different patches, which are available to lose weight, quit smoking, help to relieve stress and even increase sexuality, insect repellant patches, detoxification, male energizer, better sleeping, postpone menopause etc.

❖ **Slim herbal patch –** slim patches are 100% prepared of natural herbs and processed to soft patch form with transdermal technology. It's smooth, soft and smells slightly herbal. It is the natural way to lose weight permanently. The weight loss patch eliminates hunger while burning fat. The body slowly absorbs these elements, resulting in a "boost" to the thyroid gland. This increases the metabolism and activates fat burning mechanisms. The thyroid controls your metabolism, which in turn burns fat and decreases appetite. List of ingredients used in herbal slim patch are. Fucusvesiculosus, Guarana, 5-HTTP, Zinc Pyruvate, Flax seed oil, Lecithin, L-Carnitine, Zinc Citrate.

❖ **Anti-rheumatic herbal patch-** Rheumatic diseases affected mankind since ages and are one of the commonest inflammatory conditions in developing countries. The main ingredients used in Anti-rheumatic herbal patches are Boswellic acid and Curcumin. Ethano botanically *Boswellia* serrata*, Curcuma longa* and *Trichodesma indicum* were used for antirheumatic, anti-inflammatory and in the treatment of different skin diseases. ***Waghulkar et al.,*** **(2011)** developed the transdermal patches (films) for the antirheumatic activity by using chloroform extract of *Trichodesma indicum* and *Boswellia* serrata. Further research work also highlights on *Curcuma longa* that turmeric oil may be incorporated into the transdermal drug delivery system for their suitable and convenient use **Vishwakarma *et al.,* (2012).** Studies have shown promising results; hence, there is a scope for further pharmacodynamic and pharmacokinetic evaluation.

❖ **Cholesterol herbal patch-** TDDS is applicable to helps lower Cholesterol, Triglycerides, LDL, Lp (a) lipoprotein, and raise HDL. Side effects like flushing due to high dosage Niacin are absent when applied through Transdermal Patches without any loss in potency or efficiency. Cholesterol patches work best when taken with nutritional supplement organic magnesium on a daily basis. Briefly, one can roughly equate one 50mg Transdermal Patch to about a 500mg Oral dose taken two

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to three times a day in actual effectiveness but without the discomfort associated with oral intake. The main ingredients used in herbal cholesterol patch are Vitamin B-Complex 5mg, Niacin 20mg, Organic Vitamin C 20mg, Commiphora Mukul 20mg, Organic Chromium 100mg.

❖ **Kick the nicotine habit naturally-** The researchers have discovered a new way to combine the all-natural healing properties of a unique Variety of traditional herbal formulas to completely and naturally eliminate your body's need for nicotine. Detailed list of ingredients used in anti smoking patch are. Gotu Kola, Hops, Skullcap, Oat, Peppermint, Ginger, Gentian, Myrrh, Safflower, Eucalyptus, Licorice Root, Sarsaparilla Bayberry.

❖ **Anti-smoking patch-** This patch is a novel termination support designed to help for give up smoking safely and naturally, without putting more nicotine into the body. Its unique combine of ingredients, zero nicotine patches offers the greatest possible chance to finally drop the habit. They are applied to the skin, and put a dose of nicotine into the body.

❖ **Herbal body foot patches-**These patches are based on molecular development analysis. Molecular alteration therapy has four major components.

1) Heath Regulation - To promote mental health and health restoration

2) Increasing Oxygen intake- to enhance metabolism

3) Detoxification- To remove waste and toxins from the body

4) Balance Nutrition - To supply the body with all essential nutrients

According to Chinese medical, our human body has over 360 acupuncture points, with more than 60 acupuncture points found on the soles of the foot. When the blood circulates to the soles, the Foot Patch can absorb toxins released from the acupressure points. Circulation of blood and lymphatic fluids reach their furthest point in the soles of the feet before being return 'pumped' back up into the higher portions of the body. The body detox foot patch contains all natural ingredients, which are described as below: Bamboo Vinegar, Wood Vinegar, Tourmaline, and Eucalypt us.

❖ **Herbal plasters patches-** Plaster Patches are warm, soft, flexible, Pain Relieving Patch. Previously applied, its ingredients are absorbed into the skin to stimulate blood circulation. It's provides speedy Temporary Pain Relief and comfort for hours. Plasters are specially used in chronic or prolonged Sore Muscles, Arthritis Pain, Painful Joints, Sprains, Backache, Bruises, Shoulder Pain, Arthraiga, Rheumatic Pain, Neuralgia, and Fracture Pain. There are main two type of plaster patches are Cool plaster patch and Mild hot plaster patch. Cool plaster patch provides Rapid, Soothing Pain Relief and Alleviates swelling, with a Cool Refreshing Feeling owing to its "Cool pack effect". Patches hold a High Moisture Contents in a water-soluble Polymer Base, which enables the Deep Penetration of active ingredients in to the affected area, and provides Sustained Effects through the Continuous Release of its moisture. Caused by its Transdermal Therapeutic System, Plaster Patches can be used safely by the elderly and weak. Herbal Plasters Size 4" x 5.5" includes natural herbs like: Powdered Philodendron Bark, Capsicum Extract, Zanthoxylum Fruit, and Gardenia Fruit Methyl Salicylate.

❖ **ANTIDIABETIC ACTIVITY -** Momordica *charantia* Linn. Ethano medicinally is used as a medicine for diabetes therefore **Bhujbal *et al* (2011)** reported that M. *charantia* used for the formulation of herbal transdermal patches for the treatment of diabetes. The transdermal route exhibited negligible skin irritation and in vivo results revealed that the patches successfully decrease the blood glucose level.

LIST OF SOME EALIER REPORTED TDDS, WORKED ON BY USING SYNTHETIC DRUGS: [44, 45, 46, 47, 48, 49, 50, 51, 52]

1.ANTIDEPRESSANT ACTIVITY- Now a day's drugs like selective serotonine reuptake inhibitors (Fluoxetine, paroxetine, esitalopram, citalopram, sertaline), serotonine-norepinephrinereuptake inhibitors (venlafaxine, duloxetine),noradrenergic and specific serotonergic antidepressants (mirtazapine), nor epinephrine reuptake inhibitors (reboxetine) and nor epinephrine dopamine reuptake inhibitors (bupropion) play important role in treatment of depression. Transdermal drug delivery systems of psychotropic drugs like haloperidol, imipramine, fluoxetine, selegiline and lithium have already been studied. Transdermal drug delivery system of Selegiline, which is a monoamine oxidase inhibitor, is approved by FDA with unique pharmacokinetic and pharmacodynamic properties. This was developed to overcome limitations of orally administered MAO's, particularly dietary tyramine restrictions and was found to be suitable in long term treatment of major depressive disorder.

2. ALZHEIMER'S DISEASE-Rivastigmine is indicated for treating symptoms of mild to moderate Alzheimer's disease and dementia in Parkinson's disease as cholinesterase inhibitor. A rivastigmine patch has been developed which may provide a promising new approach to dementia therapy. It has been found that transdermal delivery of rivastigmine in patients with Alzheimer's disease significantly reduces the nausea and vomiting

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commonly associated with oral cholinesterase inhibitor therapy and is as effective as oral therapy. This patch is better tolerated by patients and is preferred by caregivers as it is easier to follow the treatment schedule and it interferes less with daily activities.

3. ANTI-INFLAMMATION ACTIVITY - Discovering a single efficient bioactive compound from ginger which possesses anti-inflammatory property with better pharmacokinetics values, in turn will create a good impact on pursuing the suitable drug delivery mode with enhanced ratio of bioavailability. The inconveniences of the standard form of drug application and side effects due to the administration route are the reason for studying the improvement strategies of bioavailability. Several active components are present in ginger among them major active ingredients are gingerol, shogaol, gingeberin and paradol. These components are used for treatment of inflammation, rheumatism, and bronchitis .The ginger extracts have been extensively studied for a broad range of biological activities including antibacterial, analgesic, anti-inflammatory, anti-tumor.

Table 1: LIST OF SOME EARLIER REPORTED RESEARCH WORK ON TRANSDERMAL DRUG DELIVERY

S.NO.	POLYMERS	RATIO	PLASTICIZER	ENHANCER	SOLVENT	DRUG	ANIMAL	PHARMACOLOGICAL ACTIVITY	REFERENCE
1	HPMC, Eudragit RL-100	2:8,4:6,8:2	Dibutylphthalate , Propylene Glycol-400	DMSO	DCM, Methanol	Amlodipine besylate	Swiss Albino Rat	Angina (hypertension)	53
2	EC (N-20), PVP (k-30)	9:1,8:2,7:3	Polyethylene Glycol-400	Methanol		Sodium diclofenac			54
3	Eudragit RS-100,Eudragit RL-100,EC		Dibutylphthalate	Oleic acid, Propylene Glycol	DCM, Ethanol	Sertraline hydrochloride	Female Mice, Rabbit	Anti-depressant	55
4	HPMC, Eudragit RL-100, EC	2:2,2:4,2:6,2:8,8:2,6:2,4:2	Propylene Glycol	DMSO, Oleic acid, Eugenol, Menthol	methanol	Simvastatin	Goat	Hypercholesterolemia	56
5	HPMC, Methylcellulose, PVP		Dibutylphthalate		DCM, Ethanol, Chloroform	Celecoxib	Rabbit, Rat, Guinea Pig, Pig ear	Anti-inflammatory analgesic	57
6	EC, HPMC	2:8,8:2,4:6,6:4	Dibutylphthalate		Methanol	Naproxen	Albino Mice	Anti-inflammatory	58
7	Na-CMC (Sodium Carboxy Methyl Cellulose)		Dibutylphthalate	Propylene Glycol		Salbutamol sulphate		Anti-asthmatic	59
8	HPMC,EC, PVP			Propylene Glycol	DCM, Ethanol	Etoricoxib	Rabbit, Rat, Guinea Pig	Gouty arthritis, Arthritis rheumatoid	60
9	HPMC, EC	2:0, 0:2,1:1	Dibutylphthalate	Dimethylsulfoxide	Methanol, Acetone	Nicardipine hydrochloride		Hypetension, Prinzmetal's varient angina	61
10	Carboxymethylchitosan, HPMC,EC	1:1,1:1.5,1:2	Glycerin, Dibutylphthalate		Chloroform	Trimetazidine hydrochloride	Rabbit	Hypoxia, Isochaemia	62
11	Sodium Alginate (SA), Xanthan Gum(XG)	10:0,8:2,6:4, 4:6,2:8	Glycerin	Menthol	Ethanol	Ketoprofen	Male Albino Rat	Joint pain, Anti-inflammatory	63
12	Chitosan, HPMC	1:3,1:5,1:7,1:9,3:1,5:1,7:1, 9:1	Dibutylphthalate		Ethanol, Dichloromethane	Metformin hydrochloride		Anti-diabetic	64
13	Chitosan, HPMC, Eudragit RL-100		Propylene Glycol	Oleic acid	glacial acetic acid,ethanol	ondansetron hydrochloride	Rat	Nausea & Vomiting	65

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14	Ethyl Cellulose, Cellulose Acetate, PVP, HPMC		Propylene Glycol	1,8-Cineole	Methanol, Acetone	Losartan	Rabbit	Anti-hypertensive	66
15	EC, Carbopol-934P, HPMC	3:1,	Propylene Glycol		Alcohol, Water	Toltero dinetartarate	Rat	Overactive bladder	67
16	Chitosan				Lactic acid		Wistar Male Rat	Anti-diabetic	68
17	Sodium Alginate (SA), Xanthan Gum(XG)		Glycerin	Menthol	Ethanol	metoprolol tartrate(MT)	Male Albino Rat	Anti-hypertensive	69
18	EC, PVP, Eudragit RL	10:0,9:1,8:2, 6:4,5:5	Dibutyl phthalate		Chloroform	Metoprolol tartrate (MT)	Rat	Hypertension	70
19	Silicone, Acrylic, Poly Acrylate	1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2,9:1	PEG-400, Propylene Glycol	Oleic acid, oils, Iso stearic acid, Pharamasolve , Isopropyl Myristate	Ethyl Acetate, Hexane, Ethylacetae,Ace ton nitrile, Methanol	Diclofenac diethylamine	Pig, Albino Rabbits, Wistar Rats	Anti-inflammatory	71
20	Polyethylene monolayer, Silicone			Labrasol, Oleic acid, Triacetin	Methanol	Diclofenac acid PSA		Anti-inflammation, Rheumatic arthritis	72
21	PVP-K30, HPMC-K-100, EC, HPMC-K4M,HPMC E15LV	1:1,1:4,3:7	PEG-400	Propylene Glycol	Water, Chloroform, Ethanol, DCM	Repaglinide	Male Wistar Rat	Diabetes mellitus	73
22	HPMC, PVP, Carbopol (CP)		Propylene Glycol		Ethanol	Glibenclamide , Atenold(β blocker)	Goat, Male Rabbit, Male Wistar Albino Rat	Diabetes and Hypertension	74
23	HPMC, Eudragit RL-100		Tri ethyl citrate		Water, Dimethyl formamide, Methanol	L ovastatin	Rabbit	Anti-lipidemic	75
24	PVP-K-30, EC	1:1, 1:2, 1:3, 1:4, 1:5	Dibutylthalate	Vegetable oils (soya bean oil, olive oil, eucalyptus oil)	Dichlorometha ne, Chloroform	Olanzapin	Wistar Male Rat	Anti-psychotic	76
25	HPMC-K4M, K15M, K100M, Na-Alginate		PEG-400		Methanol, water	Valsartan	Male Rat	Anti-hypertensive	77
26	HPMC,Eudragit-RS-100, PVP-K30,EC	9:1,8:2,7:3,	Polyethylene Glycol-400	DMSO	Chloroform,Me thanol	Glibenclamide	Mouse	Hyperglycemid e, Diabetes mellitus	78
27	Eudragit RL-100, HPMC	1.5:8.5,3:7,4: 6,6:4,7:3,8.5: 1.5	Propylene glycol, PEG-400	D-limonene	Methanol, Dichoromethan e	Lercanidipine hydrochloride (LRDP)	Albino Rat, Rabbit	Hypertension	79
28	Eudragit-RL, EC, PVP	1:3,	Dibutyl phthalate		Chloroform	Dexibuprofen	Wistar Rat, Rabbit	Inflammation	80
29	PVA,PVP, EC	10:0,9:1,8:2, 7:3,6:4 or 4:6,2:8	Dibutyl phthalate, Propylene Glycol		Water, Chloroform	Diclofenac sodium		Anti-inflammatory, Arthritis	81
30	HPMC,EC	1:4,	Glycerine, Dibutylphthalate	Olive oil, Linseed oil, Castoroil, Sunflower oil, Coconut oil, Cottonseed oil	Dichlorometha ne, Alcohol, Chloroform	Indapamide	Swiss Albino Rat	Hypertension, edema	82

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31	Sodiumcarboxymethylcellulose, PVP-k-30, EC, HPMC, Carbopol 934		Glycerol, Polyethylene Glycol		Ethanol, Glycerol	Methotrexate, Sodium alginate		Anti-cancer,Psoriasis	83
32	Carboxypolymethylene, EC	1:1,2:2,3:3,1:3,3:1	PEG-400	Turpentine oil	Chloroform,Acetone	Diclofenacdiethylamine	Rabbit	Anti-inflammatory	84
33	HPMC (K4M,K15M, K100M)	1:2,1:3,1:4	Glycerin		Water, Acetone	Enalapril maleate	Wistar Rat	Anti-hypertensive	85
34	PVP,EC		PEG-400		chloroform,Ethanol	Losartan potassium	Rat	Cardiovascular	86
35	EC, HPMC, PVP	1:2,1:4,1:6,2:1,4:1,6:1	Propylene glycol	Tween-80	Dimethyl formamide,Methanol, DMS	Nebivolol	Male Guinea Pig, Albino Rabbit	Hypertension	87
36	Eudragit RS-100, HPMC-K100M	2:8,4:6,6:4,8:2	Polyethylene glycol	DMSO	Chloroform,Methanol	Nebivolol hydrochloride	Wistar albino rat	Hypertension	88
37	Chitosan, HPMC	75:25,				Ketoprofen		Arthritis	89
38	HPMC-E5, EC	5:0,0:5,1:1	Polyethylene glycol	Tween-80	Dichloromethane, methanol	Lornoxicam		Arthritis, Anti-inflammatory	90
39	Eudragit RL-100, HPMC	5:0,4:1,3:2, 2:3,1:4	Propylene glycol	Carvone	Dichloromethane, methanol	Nitrendipine	Albino Rat	Hypertension	91
40	PVP,HPMC,EC,PVA		Propylene glycol	DMSO, Eugenol	Methanol	Propranolol hydrocloride	Rat		92

HPMC- Hydroxyl Propyl Methyl Cellulose, DMSO- Dimethylsalfoxide, EC-Ethyl Cellulose, PEG-Poly Ethylene Glycol, PVP-Poly Vinyl Pyrrolidine, CMC-Carboxy Methyl Chitosan, PVA- Polyvinyl Alcohol

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