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Research Article

Recent Advancements in Transdermal Drug Delivery System

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ABSTRACT

Transdermal drug delivery is one of the most promising methods for drug application. The administration of drugs by transdermal route offers the advantage of being relatively painless. Drug delivery with Transdermal patch systems exhibit slow, controlled drug release and absorption. Controlled drug delivery can be achieved by transdermal drug delivery system which can deliver the drug through skin to the systemic circulation at a predetermine rate over a prolonged period of time. Skin penetration enhancement technique have been developed to improve the bioavailability and increase the range of drug for which the transdermal and topical route is viable option. Characterization of transdermal patch is use to check it's quality, size, time of onset & duration, adhesive property, thickness, weight of patch, moisture of 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.

Keywords: Transdermal, Delivery, Patches, Skin.

INTRODUCTION

Transdermal therapeutic system are defined as self contained, discrete dosage form which when applied to intact skin deliver the drug through the intact skin at a control rate to the systemic circulation and maintain the drug concentration within the therapeutic window for prolonged period of time. Recently, the use of transdermal patches for pharmaceuticals is limited because only a few drugs has proven to be effectively delivered through skin, in order to achieve the objective of systemic medication through topical application to the intact skin surface. During the past few years, interest in the development of novel drug delivery systems for existing drug molecules has been renewed[1].

The development of a novel delivery system for existing drug molecules not only improves the drug's performance in terms of efficacy and safety but also improves patient compliance and overall therapeutic benefit to a significant extent[2]. When properly designed and developed for a particular drug, novel delivery system can overcome specific hurdles associated with conventional methods of delivery, e.g., drugs that undergo partial or complete degradation before reaching the site of action could be effectively delivered with improved bioavailability by using the novel concepts of timed or pulsatile release, or gastro-resistant delivery.

In this transdermal delivery system medicated adhesive patches are prepared which deliver therapeutically effective amount of drug across the skin when it placed on skin. Medicated adhesive patches or transdermal patches are of different sizes, having more than one ingredient. Once they apply on unbroken skin they deliver active ingredients into systemic circulation passing via skin barriers. A patch containing high dose of drug inside which is retained on the skin for prolonged period of time, which get enters into blood flow via diffusion process. Drug can penetrate through skin via three pathways-through hair follicles, through sebaceous glands, through sweat duct. Transdermal drug delivery systems are used in various skin disorders, also in the management of angina pectoris, pains, smoking cessation & neurological disorders such as Parkinson's disease[3].

Advantages[1,2,3,20]

Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe. The positive features of delivery drugs across the skin to achieve systemic effects are:

Transdermal medication delivers a steady infusion of the drug over prolonged period of time therefore avoiding adverse side effects and therapeutic failure frequently associated with intermittent dosing can also be avoided.

Alternative route of administration for the patients who cannot tolerate oral dosage forms such as vomiting patient.

Avoidance of first pass metabolism

Avoidance of gastro intestinal incompatibility

Predictable and extended duration of activity

Minimizing undesirable side effects

Provides utilization of drugs with short biological half lives, narrow therapeutic window

Improving physiological and pharmacological response

Avoiding the fluctuation in drug levels

Inter and intra patient variations

Maintain plasma concentration of potent drugs

Termination of therapy is easy at any point of time

Greater patient compliance due to elimination of multiple dosing profile

They are easily and rapidly identified in emergencies (for example, unresponsive, unconscious or comatose patient)

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Table 1: Marketed Products of Transdermal Drug Delivery System [1]

Sr. No.	Product	Active drug	Type of patch	Purpose	Manufacturer
1	Estraderm	Estradiol	Membrane	Postmenstrual Syndrome	Alza/Norvatis
2	Duragesic	Fentanyl	Reservoir Pain	Pain relief patch	Alza/Janseen Pharmaceutical
3	Transderm-scop	Scopolamine	Matrix Motion	Motion sickness	Alza/Norvatis
4	Deponit	Nitroglycerin	Drug in adhesive	Angina pectoris	Schwarz-Pharma
5	Lidoderm	Lidocaine	Drug in adhesive	Anaesthetic	Endo Pharmaceuticals Inc.
6	Testoderm TTS	Testosterone	Reservoir	Hypogonadism in males	Alza
7	Fematrix	Estrogen	Matrix	Postmenstrual Syndrome	Ethical Holdings/Solvay Healthcare Ltd
8	Nitrodur	Nitroglycrine	Matrix	Angina pectoris	Key Pharmaceuticals

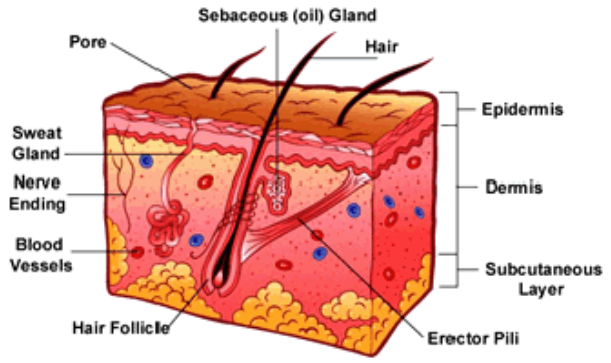

Figure 1: Structure of skin Epidermis

because of their physical presence, features and identifying markings.

Disadvantages

At the same time transdermal drug delivery has few disadvantages that are limiting the use transdermal delivery.

Only relatively potent drugs are suitable candidates for transdermal delivery because of the natural limits of drug entry imposed by the skin's impermeability.

Some patients develop contact dermatitis at the site of application from one or more of the system components, necessitating discontinuation.

The delivery system cannot be used for drugs requiring high blood levels22.

The use of transdermal delivery may be uneconomical.

Transdermal delivery is neither practical nor affordable when required to deliver large doses of drugs through skin.

Cannot administer drugs that require high blood levels.

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 barrier functions of the skin of changes from one site to another on the same person, from person to person and with age.

Anatomy and physiology of skin[4,1,2]

Skin is one of the most extensive organ of the body covering an area of about 2 m or 20 square feet on in an average human adult. This multilayerd organ receives approximately one third of all blood circulating through the body. With thickness of only a millimetre, the skin separates the underlying blood circulation network from outside environment. Human skin comprises of three clear but mutually dependent tissues: The stratified, vascular, cellular epidermis, Underlying dermis of connective tissues and Hypodermis

Human skin comprises of three distinct but mutually dependent tissues:

The stratified, vascular, cellular epidermis,

Underlying dermis of connective tissues and

Hypodermis.

Epidermis

it results from an active epithelial basal cell population

It is 100 μm thick.

It contains various layers. The stratum germinativum is the basal layer. Above the basal layer are the stratum spinosum, the stratum granulosum, the stratum lucidum, and finally, the stratum corneum (SC).

SC is the rate limiting barrier that restricts the inward and outward movement of chemical substances consists of flattened keratin-filled cells (e.g., corneocytes). Upon reaching the SC, these cells are cornified and flatten. The corneocytes are then sloughed off the skin at a rate of about one cell layer per day, a process called desquamation.

The main source of resistance to penetration and permeation through the skin is the SC.

Five layers of epidermis:

Stratum basale

Spinosum

Granulosum

Lucidum

Corneum

Dermis

It is 3 to 5mm thick layer and is composed of a matrix of connective tissue, which contains blood vessels, lymph vessels and nerves. The dermis is the inner and larger (90%)skin layer, comprises primarily of connective tissue and provides supports to the epidermis layer of the skin. The boundary between dermis and epidermis layer is

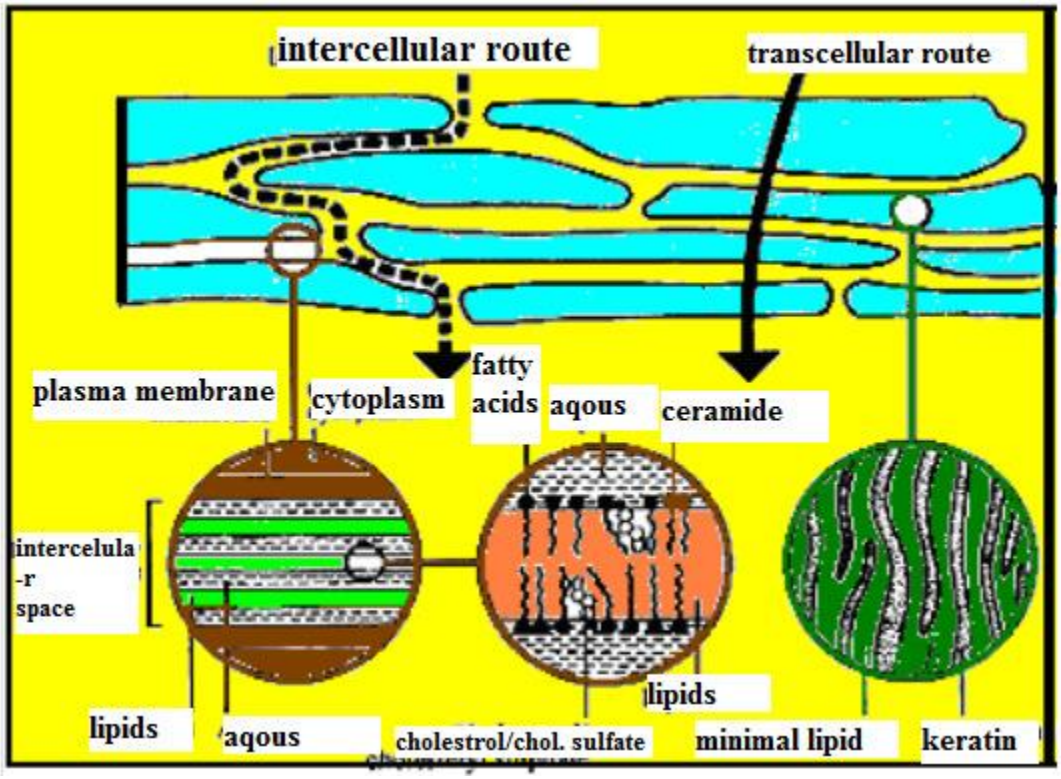

Figure 2: Epidermal route for drug permeation.

Table 2: Ideal properties of drug & some factors to be consider during preparation of TDDS.

Parameters	Properties
Dose	Should be low (less than 20mg/day)
Half life	10/less(hrs)
Molecular weight	<400da
Skin permeability coefficient	>0.5*10-3cm/h
Skin reaction	Non-irritating non-sensitizing
Oral bioavailability	Low

called Dermal- Epidermal junction which provides a physical barrier for the large molecules of drug and cells. The dermis incorporates blood and lymphatic vesicles and nerve endings. Dermis is divided into papillary & reticular region. (7)

Papillary region

It makes up one fifth of thickness of total layer, contain areolar connective tissue containing fine elastic fibers.

Reticular region

It is attached to subcutaneous layer; consist of dense irregular coactive tissue containing fibroblast, bundle of collagen & some coarce elastic fibers.

Hypodermis

The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area. This layer helps to regulate temperature, provides nutritional support and mechanic al protection. It carries principal blood vessels and nerves to skin and may contain sensory pressure organs. The hypodermis layer is composed of loose connective tissues and its thickness varies according the surface of body.

Basic principles of transdermal permeation[17]

Transdermal permeation is based on passive diffusion. Before a topically applied drug can act either locally or systemically, it must penetrate the stratum corneum – the skin permeation barrier. In the initial transient diffusion stage drug molecules may penetrate the skin along the hair follicles or sweat ducts and then absorbed through the follicular epithelium through the intact stratum corneum becomes the primary pathway for transdermal permeation. The release of a therapeutic agent from a formulation applied to the skin surface and its transport to the systemic circulation is a multistep process, which involves:

Dissolution with in and release from the formulation

Partitioning into the skin's outermost layer, the stratum corneum

Diffusion through the SC, principally via a lipidic intercellular pathway

Partitioning from the SC into the aqueous viable epidermis, diffusion through the viable epidermis and into the upper dermis, and uptake into the papillary dermis and into the microcirculation

Factors affecting transdermal permeation[2 17,18]

Physicochemical properties of the penetrant molecules

Partition coefficient

A lipid/water partition coefficient of 1 or greater is generally required for optimal transdermal permeability. It may be altered by chemical modification without affecting the pharmacological activity of the drug.

pH conditions

Applications of solutions whose pH values are very high or very low can be destructive to the skin. With moderate pH values, the flux of ionizable drugs can be affected by

changes in pH that alter the ratio of charged and uncharged species and their transdermal permeability.

Penetrant concentration

Assuming membrane related transport, increasing concentration of dissolved drug causes a proportional increase in flux. At concentration higher than the solubility, excess solid drug functions as a reservoir and helps maintain a constant drug constitution for a prolonged period of time.

Physicochemical properties of the drug delivery system

Release characteristics

Solubility of the drug in the vehicle determines the release rate. The mechanism of drug release depends on the following factors:

Whether the drug molecules are dissolved or suspended in the delivery systems.

The interfacial partition coefficient of the drug from the delivery system to the skin tissue.

pH of the vehicle

Composition of the drug delivery systems

The composition of the drug delivery systems e.g., boundary layers, thickness, polymers, vehicles not only affects the rate of drug release, but also the permeability of the stratum corneum by means of hydration, making with skin lipids, or other sorption promoting effects e.g., benzocaine permeation decreases with PEG of low molecular weight.

Skin (Transcorneal) penetration[1,19]

Intra cellular penetration

Drug molecule passes through the cells of the stratum corneum. It is generally seen in case of hydrophilic drugs. As stratum corneum hydrates, water accumulates near the outer surface of the protein filaments. Polar molecules appear to pass through this immobilized water.

Intercellular penetration

Non-polar substances follow the route of intercellular penetration. These molecules dissolve in and diffuse through the non- aqueous lipid matrix imbibed between the protein filaments.

Transappendegeal penetration

This is also called as the shunt pathway. In this route, the drug molecule may transverse through the hair follicles, the sebaceous pathway of the pilosebaceous apparatus or the aqueous pathway of the salty sweat glands. The transappendegeal pathway is considered to be of minor importance because of its relatively smaller area (less than 0.1% of total surface).

The transdermal permeation can be visualized as composite of a series in sequence as:

Adsorption of a penetrant molecule onto the surface layers of stratum corneum.

Diffusion through stratum corneum and through viable epidermis.

Finally through the papillary dermis into the microcirculation.

The viable tissue layer and the capillaries are relatively permeable and the peripheral circulation is sufficiently rapid. Hence diffusion through the stratum corneum is the rate-limiting step. The stratum corneum acts like a passive diffusion medium. So, for transdermal drug diffusion, the various skin tissue layers can be represented by a simple multilayer model as shown in Figure.

Components of transdermal drug delivery system [3,21]

Polymer matrix/ Drug reservoir

Drug.

Permeation enhancers.

Pressure sensitive adhesive (PSA).

Backing laminate.

Release liner.

Other excipients like plasticizers and solvents

Polymer matrix/ Drug reservoir

Polymers are core part of TDDS. It is prepared by dispersing the drug in liquid or solid state synthetic polymer base. Polymers used in TDDS should have biocompatibility and chemical compatibility with the drug and other components of the system such as penetration enhancers. Additionally, they should provide consistent and

effective delivery of a drug throughout the product's intended shelf life and should be of safe status. Polymers used in TDDS are classified as-

Natural Polymers: e.g. cellulose derivatives, gelatin, shellac, waxes, gums, and chitosan etc.

Synthetic Elastomers: e.g. poly butadiene, poly isobutylene, silicon, nitrile, acrylonitrile, neoprene, butyl rubber etc.

Synthetic Polymers: e.g. polyvinyl alcohol, polyvinylchloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, poly vinyl pyrrolidone, polymethyl methacrylate etc[22].

Drug

Some of ideal properties of drug & some factors to be consider during preparation of TDDS are as follows-

Permeation enhancers[3]

Chemical compounds that increase permeability of stratum corneum so as to attain higher therapeutic levels of the drug candidate. They improve the permeability by interacting with structural components of stratum corneum.

Ideal properties of permeation enhancers-

They should be non-irritating, on toxic & nonallergic.

They should not bind to receptor site i.e. not showing any pharmacological activity.

They should be cosmetically acceptable with an appropriate skin feel[14].

Pressure sensitive adhesive (PSA)

Pressure sensitive adhesive helps to adhere transdermal patch to the skin surface. It can easily remove from the smooth surface without leaving a residue on it. Ex- Polyacrylates, polyisobutylene and silicon based adhesives are widely used in TDDS.

Backing laminate[7]

Backing laminates are supportive material which is impermeable to drugs and to permeation Enhancers. They should chemically compatible with the drug, enhancer, adhesive and other excipients. Ex-vinyl, polyethylene and polyester films.

Release liner[8]

Release liner is the primary packaging material that can protect the patch which will remove during application of

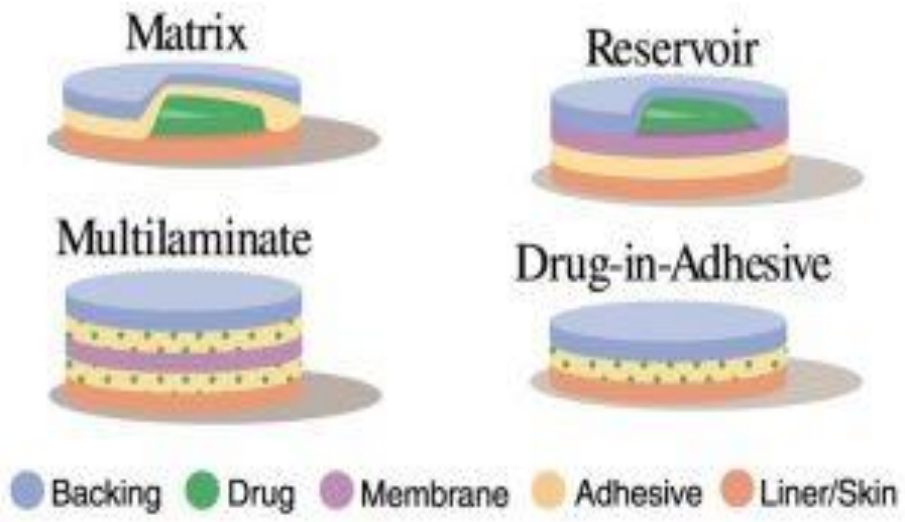

Figure 3: Types of Transdermal Patches.

patch to the skin. Release liner is made up of base layer which may be non-occlusive (e.g. paper fabric) or occlusive (e.g. polyethylene, polyvinylchloride) and a release coating layer made up of silicon or Teflon. Release liner should be chemically inert & it should be permeable to drug, penetration enhancers & water.

Other excipients like plasticizers and solvents

Solvents used are chloroform, methanol, acetone, isopropanol and dichloromethane. Plasticizers used dibutylpthalate, triethylcitrate, polyethylene glycol and propylene glycol[8].

Types of transdermal drug delivery system[5,23]

Reservoir System

In drug this System the drug reservoir is kept in between backing layer and a rate controlling membrane. Drug releases through microporous rate controlled membrane. Drug can be in the form of a solution, suspension, or gel or dispersed in a solid polymer matrix in the reservoir compartment.

Matrix System

Drug-in-adhesive system- For the formation of drug reservoir drug dispersed in an adhesive polymer and then spreading the medicated polymer adhesive by solvent casting or by melting the adhesive (in the case of hot-melt adhesives) onto an impervious backing layer.

Matrix-dispersion system

In matrix-dispersion system the drug is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. Then this containing polymer along with drug is fixed onto an occlusive base plate in a compartment fabricated from a drug-impermeable backing layer. Adhesive is spread along the circumference instead of applying on the face of drug reservoir to form a strip of adhesive rim[9].

Micro-Reservoir System

This system a combination of reservoir and matrix-dispersion systems. Here drug is suspended in an aqueous solution of water-soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unbleachable, microscopic spheres of drug reservoirs[10].

Types of transdermal patches[2,11,24]

Four major transdermal systems

Single–layer drug in–adhesive

The adhesive layer of this system also contains the drug. In this type patches the adhesive layer not only serves to adhere the various layer together, along with entire system to the skin but is also responsible for the releasing of the drug. The adhesive layer is surrounded by a temporary liner and a backing.

Multi-layer drug in adhesive

The multi-layer drug in adhesive is like the single layer system in that both adhesive layer are also responsible for the releasing of the drug. But it is different however that it adds another layer of drug in – adhesive, usually separated by a membrane. This patch also has a temporary liner – layer and a permanent backing.

Drug reservoir-in-adhesive

Reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension separated by the backing layer. In this type of system the rate of release is zero order.

Drug matrix-in-adhesive

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

Recent technology used in transdermal drug delivery system[4,12]

Iontophoresis.
Electroporation.
Microneedle-based Devices.
Abrasion
Needle-less Injection
Laser Radiation
Microporation
Needleless injection

Evaluation of transdermal system[4,13,14,15]

Interaction studies

The drug and polymer compatibility was characterized by means of FTIR spectroscopy. The compatibility was checked by making physical mixture of drug and polymer

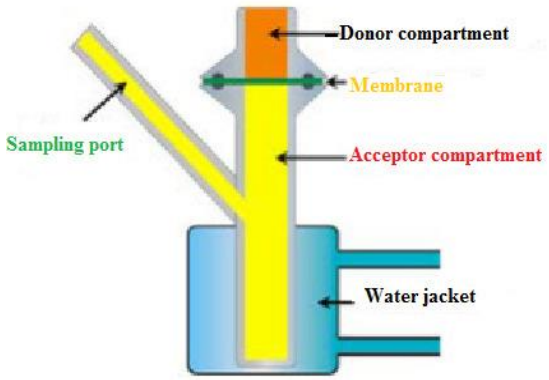

Figure 4: Franz Diffuse Cell.

(1:1) and then the FTIR analysis of the mixture was done. The peaks should not be changed in FTIR spectra of mixtures, and it should be similar to the pure drug and polymer FTIR spectra. Evaluation is of three types: Physicochemical evaluation, Invitro studies and In vivo studies.

Physical or physicochemical evaluation of transdermal system

Film thickness

This is measured by using micro meter, electronic vernier callipers, with a least count of 0.01mm, dial gauge, or screw gauge. Thickness is measured at five different points on the film and average of five readings is taken.

Percentage flatness

Strips are selected as the average per cent of length calculated from the 7 cm strips. Zero percent constriction is equivalent to 100 percent flatness. % Constriction = (initial length-final length)/initial length *100

Folding endurance

It is determined by repeatedly folding a small strip of film (2 x 2 cm) at the same place till it breaks. The number of time the film could be folded at the same place without breaking is the folding endurance value.

Tensile strength

It is determined by using a modified pulley system. The force required to break the film is considered as tensile strength and it is measured as kg/cm2.

Patch thickness

It is measured by using digital micrometre screw gauge at three different points and calculation of mean value is done.

Elongation break test

It is determined by noting the length just before the break point. The elongation break can be calculated by the formula: Elongation break = (final length-initial length)/initial length.

Weight uniformity

weight uniformity is studied by randomly selecting patches 10 in number. A specified area of patch is to be cut in different parts of the patch and weighed in a digital balance. Calculate average weight and standard deviation value from the individual weights. It is performed for each formulation.

Drug content

A film of required area (1 x1 cm / 2 x 2 cm etc.) is cut, place small piece of film in to 100 ml buffer (pH 7.4 or 6.8 or as prescribed) and shake continuously for 24 hours. Then the whole solution is ultrasonicated for 15 minutes. And filtration is done, then the drug is estimated spectrophotometrically and the drug content is determined.

Percentage of moisture content

Individually films are weighed and left in a desiccator containing anhydrous calcium chloride or activated silica at room temperature for 24 hours. They are weighed individually until they show constant weight. Calculation of % of moisture content is done as the difference between initial and final weight by the final weight. % moisture Content= [initial weight-final weight]/final weight *100.

Percentage of moisture uptake

A weighed film is a kept in desiccator at room temperature for 24 hours and taken out and 84% relative humidity (a saturated solution of potassium chloride) in a desiccator and the films are exposed to it until a constant weight is obtained. The percentage of moisture uptake is calculated as the difference between the final and initial weight by initial weight. % moisture uptake= [final weight-initial weight]/initial weight *100.

Water vapour transmission rate

Glass vials approx. 5 ml capacity of equal diameter are taken for transmission study. All vials are washed thoroughly and dried in an oven completely. Weigh about 1 gm of anhydrous/ fused calcium chloride and kept in all the taken vials. Films are fixed on the brim of vials and weighed individually then keep in closed desiccator containing saturated solution of potassium chloride to maintain humidity approx. 84%. The vials were weighed at 6, 12, 24, 36, 48 and 72 hours respectively. WVP is calculated in gm/m2 per 24hrs Transmission rate= [(final weight-initial weight)/area*time] * 100.

Adhesive studies

Shear adhesion test

This test is used to determine the cohesive strength of an adhesive polymer. The strength value is affected by the degree of cross linking, the molecular weight, the composition of polymer and the amount of tackifiers used. An adhesive coated patch is stacked between the plate made of stainless steel and specified weight hung from the patch parallel to this plat. The time taken to pull off this patch is the cohesive strength. Greater the strength more is the shear strength

Peel adhesion test

The measurement of patch strength between an adhesive and a substrate is defined as adhesion. The force required for removing adhesive coating from the steel used as test substrate. The type and amount of polymer, the molecular weight and the composition of polymers determine the adhesive properties. The single patch is pasted to test substrate (Steel) and it pulled from the substrate at 180o angle. Failure of adhesive is indicated with no residue on substrate.

Tack properties

Tack is the ability of polymer to adhere to a substrate with little contact pressure. Application with little finger pressure is important in transdermal systems. Tack is

dependent on molecular weight as well as composition of polymer and tackifying resins used in the polymer.

Tests for tack include

Thumb tack test
Rolling ball tack test
Peel tack or quick stick test
Probe tack test

In vitro drug release studies

For the assessment of the release of the drug from the patches the paddle over disc method (USP apparatus V) can be used. Here the film with defined thickness, shape taken, weigh it, fixed over glass plate attached with adhesive. It is kept in 500ml phosphate buffer (pH7.4) as dissolution media & set the apparatus at 32±0. 5°C.Keep the paddle at a distance 2.5cm from the glass plate & operated at a speed of 50rpm.5ml of sample can withdraw at specific time interval for 24hrs & analysed by UV or HPLC.Perform the experiment in triplicate.

In vitro skin permeation studies

By using diffusion cell in vitro skin permeation study is carried out. Here use of male wistar rat weighing 200-250gm. Take the abdominal skin of rat by removing the hairs from abdominal region by using electric clipper. Then dermal side of the skin is washed with distilled water to remove adhesive tissues then it is kept in dissolution media or phosphate buffer pH 7.4 for 1hr. before starting the experiment & was placed on magnetic stirrer with small magnetic needle for uniform distribution of diffusant. The temperature of cell was maintained at 32±0.5°C using thermostatically controlled heater. Rat skin is placed between the compartment of diffusion cell with epidermis facing in upward into donor compartment. Specific amount of volume is withdrawn from receptor compartment at specific time interval & equal volume of fresh sample is add. Withdraw sample is filtered& analysed by UV or by using HPLC.Flux can be determined by plotting the slop between steady state values of the amount of drug permeated mg cm2vs. time in hours & permeability coefficient were deduced by dividing the flux by initial drug load mg cm2.

Skin irritancy studies

The skin irritancy can be performed on healthy rabbits / mice albino / rats and potential of transdermal system can be evaluated by modified Draize test. Clean and remove the hair from the dorsal surface of test animal and clean surface then apply rectified spirit. Apply the transdermal formulation over the clean surface for 24 hours.

Stability studies

Stability studies were done as per ICH guidelines where TDS samples are stored at 40 ± 0.5°C and 75 ± 5% RH for 6 months. The samples were withdrawn at 0, 30, 60, 90 and 180 days and analysed suitably for the drug content (Singh et al., 1993).

Recent Technology Used in Transdermal Drug Delivery System

Iontophoresis

This method involves the application of a low level electric current either directly to the skin or indirectly via the dosage form in order to enhance permeation of a topically applied therapeutic agent19, 20. Increased drug permeation as a result of this methodology can be attributed to either one or a combination of the following mechanisms: Electro-repulsion (for charged solutes), electro osmosis (for uncharged solutes) and electro-perturbation (for both charged and uncharged). Several iontophoretic systems are currently under commercial development including the Phoresor device developed by Iomed Inc. and the Vyteris and E-TRANS devices developed by Alza Corp.

Electroporation

This method involves the application of high voltage pulses to the skin which has been suggested to induce the formation of transient pores. High voltages (100 V) and short treatment durations (milliseconds) are most frequently employed. Other electrical parameters that affect permeation rate include pulse properties such as waveform, rate and number. The technology has been successfully used to enhance the skin permeability of molecules with differing lipophilicity and size (i.e. small molecules, proteins, peptides and oligonucleotides) including biopharmaceuticals with molecular weights greater than 7kDA.23.

Microneedle-based Devices

The very first microneedle systems, described in 1976, consisted of a drug reservoir and a plurality of projections (microneedles 50 to 100 mm long) extending from the reservoir, which penetrated the stratum corneum and epidermis to deliver the drug. The ALZA Corp. has recently commercialized a microneedle technology named Macro flux which can either be used in combination with a drug reservoir or by dry coating the drug on the micro projection array24, the latter being better for intracutaneously immunization.

Abrasion

The abrasion technique involves the direct removal or disruption of the upper layers of the skin to facilitate the permeation of topically applied medicaments. Some of these devices are based on techniques employed by dermatologists for superficial skin resurfacing (e.g. microdermabrasion) which are used in the treatment of acne, scars, hyperpigmentation and other skin blemishes.

Needle-less Injection

This is reported to involve a pain-free method of administering drugs to the skin. Over the years, there have been numerous examples of both liquid (Ped-O-Jet, Iject, Biojector2000, Medi-jector and Introject) and powder (PMED device formerly known as Powderject injector) systems. The latter device has been reported to successfully deliver testosterone, lidocaine hydrochloride and macromolecules such as calcitonin and insulin. Of ultrasonic energy to enhance the transdermal delivery of solutes either simultaneously or via pre-treatment and is frequently referred to as sonophoresis or phonophoresis. The SonoPrep device (Sontra Medical Corp.) uses low frequency ultrasound (55 kHz) for an average duration of 15 seconds to enhance skin permeability. This battery-operated, handheld device consists of a control unit, ultrasonic horn with control panel, a disposable coupling medium cartridge, and a return electrod.

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.

Iontophoretic Drug Delivery System

"Iontophoresis can be defined as the permeation of ionized drug molecules across biological membranes under the influence of electrical current." Iontophoresis implies the use of small amount of physiologically acceptable electric current to drive ionic (charged) drugs into body by using an electrode of the same polarity as the charge on the drug; the drug is driven into the skin mainly by electrostatic repulsion. The technique has been observed to enhance the transdermal permeation of ionic drugs several folds and this proposed to expand the horizon of transdermal control drug delivery for systemic medication. Beside the usual benefit of transdermal drug delivery, iontophoresis present a unique opportunity to provide programmed drug delivery. This is because the permeation rate is proportional to the current density, which can be readily adjusted. Such dependence on current may also make drug absorption via iontophoresis less dependent on biological variables.

Needleless injection

Needleless injection involves a pain-free method of administration of drugs to the skin. This technique involves firing the liquid or solid particles at supersonic speeds through the stratum corneum. Problems with this technique include the high developmental cost for both the device and dosage form and the inability to program or control drug delivery to compensate for inter subject differences in skin permeability. Needleless injection – Mechanism The mechanism involves forcing compressed gas such as helium or nitrogen through the nozzle with the resultant drug particles entrained within the jet flow, reportedly traveling at sufficient velocity for skin. penetration.

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