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REVIEW ARTICLE **OPEN ACCESS**

Dermal Patches: A Review

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ABSTRACT

Dermal patches are also term as Skin patches, and it is a medicated adhesive patch used to place on skin to deliver a medication into the skin and not in a bloodstream. There are several uses of patches, some patches are used to deliver NSAID drug for treatment of acute pain due to minor strains, and contusions. Some patches are used for treatment of Inflammation and acts as an anti-inflammatory patch. These patches are used for treatment of Arthritis. Some patches are used to relieve the peripheral pain that contains drugs like lidocaine. These patches are used to treat chronic pain associated with some major injuries. Recently some dermal skin patches are also used after commercial skin grafting cases. In that case antibiotics are major drug molecules embedded in it. Dermal patches now used for many purposes and some new patches are approved recently for dermal applications. This review paper is focused on about introduction of dermal patches, its method of preparation, its in-vivo and in-vitro test and its applications.

Keywords: *Dermal Patches, Anti-inflammatory, Antibiotics*

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INTRODUCTION

With an area of 1.5 to 2.0 m2 in adults, the skin is the biggest organ in the human body by mass. To treat superficial disorders, drugs have been administered to the skin [1].There are a variety of administration methods depending on the delivery route, including oral administration, transdermal administration, lung inhalation, mucosal administration, and intravenous injection [2]. Oral administration is the most common method of medication administration but it has several drawbacks, such as drug absorption variability, first-pass metabolism, drug degradation, and the possibility of drug destruction by digestive enzymes and stomach acid. Chien, Banker, and Guy devised a unique medication delivery mechanism to solve this challenge in 1992, 1990, and 1996, respectively. It was dermal Patches [3]. A dermal patch, also known as a skin patch, is a medicated adhesive patch that is applied to the skin to deliver medication. A transdermal patch, on the other hand, delivers the medication through the skin and into the bloodstream [4].Compounds are stored in the reservoir within the patches, which is sticky to the skin on one side and has an impermeable backing on the other [5]. The medications dissolved or dispersed in a reservoir or inert polymer matrix; an exterior backing sheet of paper, plastic, or foil; and pressure sensitive adhesive that attaches the patches to the skin are the core components of any dermal administration system. The adhesive is covered with a release liner that must be peeled away before the patch can be applied to the skin[6].

Ideal drug candidates for dermal drug delivery system require the following characteristics [7,8]

Molecular weight should be	< 500 Da
Log Partition Coefficient	1-3
Potent molecule dose	< 10 mg
Aqueous Solubility	>100 ug/ml
Melting Point	< 200°C
pH of aqueous saturated solution	5-9
Skin Reaction	Non irritating, Non sensitizing

Dermal Patch System Types

Drug-in-Adhesive System with a Single Layer: The medicine is included in the adhesive layer of this sort of patch. A backing layer and a drug-in-adhesive (DIA) layer make up this patch method. The DIA patch also comes with a liner that covers the DIA layer and must be removed before to use. Patches are often thinner, lighter, and more flexible than reservoir systems, allowing for improved skin conformability [1,9].

Reservoir System: The reservoir system is made up of four main components a backing layer, a drug reservoir, a rate-control membrane, and a drug-in-adhesive layer. This technique is intended for drug distribution over a longer period of time. After passing through the membrane and diffusing through the drug –in-adhesive layer, the drug in the drug reservoir would come into touch with the skin. Risk of reservoir patch system was dose dumping of large amount of medicine when exposed to specific condition[1, 10].

Matrix system: This system is of two types[11,12]

a) Drug-in-adhesive System: The drug is dispersed in an adhesive polymer, and the medicated polymer adhesive is distributed by solvent casting or melting the adhesive (in the case of hot-melt adhesive) on to an impermeable backing layer to produce a drug reservoir.

b) Matrix-Dispersion System: The medication is disseminated uniformly in a hydrophilic or lipophilic polymer matrix in this system. And the drug-containing polymer is attached to an occlusive base plate in a compartment made of a drug-impervious backing layer. Instead of applying adhesive to the front of the drug reservoir to produce a strip, the adhesive is dispersed around the circle with this approach[13].

Micro-Reservoir System: This method incorporates a reservoir and a matrix-dispersion system into one. In this method, the drug is suspended in an aqueous solution of a water-soluble polymer before being homogeneously dispersed in a lipophilic polymer to generate thousands of unbleachable, microscopic drug reservoir spheres[14]

Method of Preparation of Dermal Patch

a) Asymmetric TPX membrane method
b) Circular Teflon mould method
c) Mercury substrate method
d) By using IPM membrane method
e) By using " EVAC membrane" method
f) Preparation of TDDS by using Proliposome
g) By using free film method

a) Asymmetric TPX membrane approach: Berner and John discovered this technology in 1994. Drug is disseminated on a concave membrane, which is then covered by an asymmetric TPX [poly (4-methyl-1-pentene)] membrane and sealed with an adhesive. Preparation: The dry or wet inversion procedure is used to make them [3]. To make a polymer solution, TPX is dissolved in a mixture of solvent (cyclohexane) and non-solvent additive at 60^0C. The polymer solution is maintained at 40 ^{0}C for 24 hours before being cast on a glass plate[3,15]. The casting film is then evaporated for 30 seconds at 50^0C, and the glass plate is immediately immersed in the coagulation bath (at 25^0C). The membrane can be removed after 10 minutes of immersion and dried in a circular oven at 50^0C for 12 hours [16].
b) Banker and Heller discovered the circular Teflon Mould Method in 1989. In an organic solvent, a solution containing polymers in various ratios is utilised. The amount of medicine calculated is dissolved in half the amount of the same organic solvent [6,7]. In the drug polymer solution, a plasticizer is added. The entire mixture must be mixed before being put into the round Teflon mould. With an inverted glass funnel on a Teflon mould, the rate of solvent vaporisation can be adjusted. For 24 hours, the solvent is allowed to evaporate. The desiccator will be used to store the dried films[15,16].
c) Mercury Substrate Method: The medication and plasticizer dissolve in the polymeric solution. It was stirred for 10-15 minutes to generate a homogeneous dispersion, then poured into a flat mercury surface and covered with an inverted funnel to keep the solvent from evaporating[16,17].
d) By Using IPM Membrane Method: The medication is distributed in a mixture of water and propylene glycol containing carbomer 940 polymer and agitated in a magnetic stirrer for 12 hours[15,16]. With the addition of triethanolamine, the dispersion will be neutralised and viscous. If the drug's solubility in aqueous solution is poor, a buffer pH 7.4 can be employed to make a solution gel. The IPM membrane will incorporate the formerdgel[6,17].
e) By using "EVAC membrane" method: 1% carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membrane can be employed as rate control membrane to prepare the target dermal therapeutic system [6,7]. Propylene glycol is utilised to make the gel if the drug is not soluble in water. The drug will be dissolved in propylene glycol, then carbopol resin will be added and neutralised with a 5 percent w/w sodium hydroxide solution [15,16]. The medicine (in gel form) is applied to a backing layer sheet that covers the desired area. To make a leak-proof

device, a rate-controlling membrane will be placed over the gel and the borders will be sealed with heat[17].

f) Preparation of DDS by using Proliposome: Proliposomes are made with the carrier method and the film deposition technique [6]. The drug-to-lecithin ratio should be 0.1:2.0, as suggested by earlier research[7]. To make Proliposomes, put 5 mg of mannitol powder in a 100 ml round bottom flask, keep it at 60-70^{0}C, rotate it at 80-90 rpm, and vacuum dry it for 30 minutes. The water bath temperature is raised to 20-30^{0}C after drying. The drug and lecithin are dissolved in a suitable organic solvent mixture, and a 0.5 ml aliquot of the organic solution is added to the round bottomed flask at 37^{0}C after complete drying. After the last loading, the flask contain Proliposome are connected in the lyophilizer and subsequently drug loaded mannitol powders (Proliposome) are placed in a dessicator overnight and then sieved through 100 mesh. The collected powder is transferred into a glass bottle and stored at the freeze temperature until characterization [15,16].

g) By using free film method: Casting on a mercury surface produces a free cellulose acetate film[6,7]. Chloroform is used to make a 2 percent w/w polymer solution. Plasticizers are added at a concentration of 40% by weight of the polymer. In a glass petri dish, 5 mL of polymer solution was put into a glass ring that was positioned over the mercury surface. Placing an inverted funnel over a Petri dish controls the pace of solvent evaporation[16].Observing the mercury surface after the solvent has completely evaporated reveals the 1ml formation. The dried 1ml will be separated and stored in a desiccator between wax paper sheets until needed. By varying the volume of the polymer solution, free films of various thicknesses can be created[17].

Test for Dermal Patch

***In-vitro* permeation studies:** If rat skins are used, the K-C cell (Keshary-chein) diffusion cell is used. Before running the experiment, hairless skin is thoroughly cleaned of any adhering tissue or blood vessel and equilibrated for an hour in pH 7 buffer[7]. The K. C. cell or skin piece was placed between the diffusion cell compartment and the donor compartment, with the epidermal part of the skin facing upward or toward the donor compartment. The patch that will be tested will be applied to the skin [15,16]. The receptor phase is a specific butter medium that is swirled with a magnetic stirrer at 37^{0}C + 1^{0}C. A specific amount of sample was taken from the sampling port on a regular basis, and new receptor fluid was introduced. Sample absorbance measured spectrophotometrically in comparison to a blank. The cumulative amount of drug permeated is plotted against time in hour [19,20].

***In-vitro* drug release studies**: The release of medication from patches was assessed using a modified dissolution apparatus consisting of a jacketed vertical glass beaker 18 cm long and 48 cm in diameter [15]. The specific amount of buffer solution composition. The patch to be examined is placed in a glass beaker containing the dissolution media and struck on to a depression (15mm internal diameter and 1.5mm depth) on a Teflon block made for the purpose. The apparatus was set to 37^{0}C + 20^{0}C and ran at 50 revolutions per minute. Out of a regular interval of time, a specific amount of sample pipette is taken. The material is filtered out using filter paper and then membrane filtered before being analysed using HPLC or UV spectrophotometer [18,19].

***In-vivo* method:** 1) Animal model 2) Human Volunteers Animal model can be used to evaluate the dermal patch *in vivo* [18,19]. Because human research takes a long time and demand a lot of resources, in vivo animal models are chosen. Mouse, rat, guinea pig, rabbit, cat, dog, pig, monkey, or rhesus monkey is some of the species used in in vivo evaluation of dermal patches standard radiotracer approach. The abdomens, which are the least hairy part of the animal's body, are usually the application site [19,20].

MORPHOLOGICAL AND PHYSICOCHEMICAL CHARACTERIZATION OF THE PATCHES

Microscopic Morphological Observation: Scanning electron microscopy is used to study dry areas that have been coated with a gold coating [20]. SES pictures are used to create a histogram of the diameter of roughly 50 individual pores. Per group, three samples are evaluated. The mean patch diameter was used to calculate the effective diameters of the pores [21].

Melting Point: Place a small amount of drug in a capillary tube with a fused end in a melting point instrument and record the melting temperature. And then take three separate measurements and average them out [20,21].

Fourier Transform Infrared Spectroscopy [FTIR]: Using the KBr pellets approach, Fourier transform infrared spectroscopy was used to analyse the pure drug, drug and other ingredient mixture, and drug loaded dermal patch (a few mg of the sample and excess of KBr are finely ground and pressed under high pressure into the pellet). From 400 to 4000 cm-1, the entire sample is scanned [20].

Differential Scanning Calorimetry: DSC thermograms of the pure drug and the formulation are used to look for possible interactions between the medication and the polymer [20]. The entire sample is enclosed

in flat-bottomed aluminium pans and heated at a rate of 5^0C/min throughout a temperature range of 25 to 300^0C [21].

Weight Loss Assay: 1 mL distilled water is added to each weight patch, and the mixture is incubated at room temperature for 3, 6, 12, 24, and 48 hours. Before being weighed, the samples are blotted dry[21]. The water retention percentage is calculated as (Wt – Wi)/Wi 100 percent, where Wi is the beginning weight and Wt is the weight after a given period of submersion in distilled water [22].

Drug Release Assay:1mg of dermal patch which contained active ingredient at concentration 1mh/ml, and active ingredient at concentration 2.4mg/ml are soaked in 1ml of distilled water for 0.5,1,2,4,6,8,10 and 12 h respectively. Each sample is then analysed via UV-Vis spectroscopy at 325nm. The concentration of drug release is calculated by using the formula of absorbance against concentration. The drug release rate is calculated by formula given below

Drug release rate (%) = the amount of release drug (mM)/the amount of drug in the patch (mm)[20].

***In-Vitro* Cell Viability Assay:** The dermal patch with the different concentration of active ingredient in triplicate is soaked individually in 1ml of the culture medium for 3, 6, 12, 24 and 48 h. As a control, a dermal patch with no active component was employed. In a flat bottom tissue culture plate, the cells are cultured in triplicate. WST-1 cell proliferation colorimetric assay is used to assess cell viability[20].

Antibacterial Activity Assay: Disk diffusion analysis is used to determine antibacterial activity. The patch is seeded with S. aureus, P. aeruginosa, and E. coli on an LB agar plate. The inhibitory zone diameter is measured after 16 hours of incubation at 37^0C. Each assay is carried out three times in triplicate[20].

APPLICATION OF DERMAL PATCH

Acne Treatment: Acne is a long-term inflammatory skin condition characterised by comedones, papules, and nodules. The majority of acne patches in the market contain hydrocolloids and salicylic acid[23]. Hydrocolloid isn't a filler that's put on a sticker to produce an acne patch; it's a substance that acts as the adhesive[24]. Gel forming agent, pectin, and gelatin are used to make it. The substance in hydrocolloids actively absorbs fluid and pus without drying the surrounding skin, which was originally created to treat wounds. It's also effective against acne. Aloe, tea tree oil, salicylic acid, and benzoyl peroxide are among the other components[20,24].

Wound Treatment: Skin serves as a vital line of defence against a variety of injuries. However, a variety of circumstances, such as physical damage and infections, might jeopardise the skin's integrity [25]. A wound is a break or a flaw in the skin tissue[26]. Traditional wound dressings comprised of absorbent cotton and gauze serve an important role in wound healing, but due to a lack of timely monitoring capability, they are unable to signal the infection status of the wound [27].

Wound patches have received a lot of attention in recent years because of their unique benefits such flexibility, real-time monitoring, non-invasiveness, disposableness, high integration, high sensitivity, and high stability[28]. To help prevent infection and keep the area moist, drugs like Bacitracin and Neosporin are used[29,30].

Tan Removal Treatment: When ultraviolet (UV) radiation from the sun or artificial UV rays strike the skin, a pigment called melanin is formed. Melanin is the pigment that gives tans their brown glow[31,32]. Vitamin C patches and masks decrease melanin formation in the skin, which helps to eliminate hyperpigmentation and dark spots, even skin tone, and improve brightness. Meladermthepary uses Glycolic Acid[33]. It promotes the formation of natural collagen in the skin. Glycolic acid patch/mask improves blood flow and minimises uneven skin tone. Niacinamide patch/mask brightens the skin and inhibits melanin production, reducing the appearance of hyperpigmentation such as dark patches, acne scars, and discolouration[33,34].

Treatment of Pain Relief:A pain relief patch can aid with pain relief. The patches are applied to your skin and allow the natural extract or medicinal component to infiltrate the epidermis, providing relief from skin irritation[35]. In the market, there are certain heat patches that provide heat to the affected area and help you feel better. Delayed onset muscular soreness is treated with a Menthol Patch (DOMS). For several days, the presence of DOMS reduces muscular activity[36]. Flector (diclofenac epolamine) is a pain reliever. Non-steroidal anti-inflammatory drugs (NSAIDs) are a type of medication that belongs to the NSAID class of drugs (NSAID). Pain alleviation should be felt within an hour of placing the usual pain patch[36,37]. Some pain patches, on the other hand (pain patches that interact with your body's electrical signals), operate in seconds. Pain patches can last anywhere from 4 to 12 hours, 8 to 12 hours, 24 to 48 hours, depending on the manufacturer. Camphor, methanol, cananabidiol (CBD), and methylsalicylate are all included in some pain treatment patches [35,36].

Treatment of Fungal Infection: Dermatophytosis has become the fourth most frequent condition in the last decade, affecting 20 to 25 percent of the global population. Infection with a fungus People who live in

hot or humid climates are more likely to have nail infections. Nail infection is treated with a dermal patch containing ciclopiroxolamine[38].

Treatment of Skin Whiting: Glutathion is a cellular molecule that aids in the detoxification of waste products and certain drug contaminants. It's also an antioxidant, which helps cells combat damage caused by free radicals, which are destructive compounds [38].Because the body breaks glutathione down into amino acids, it is poorly absorbed from meals. Glutathion patches help to lighten skin and minimise hyperpigmentation, especially in ethnic populations with darker skin tones. Glutathione, dubbed the "Magical Skin Whitening" molecule in nations like the Philippines, has exploded in popularity around the world in a short period of time[39,40]. Collagen patches comprise collagen (a natural skin protein that supports skin firmness, suppleness, and elasticity) and peptides (proteins that assist support skin firmness, suppleness, and elasticity) (Peptides are short chains of amino acids that act as building blocks of protein such as collagen, elastin, and keratin) Hyaluronic Acid is a kind of hyaluronic acid (This hydration booster hold 1000X its weight in water and prevents moisture loss at the cellular level, giving you a perfectly quenched and nourished look). Collagen patches aid in the reduction of fine lines and wrinkles, as well as the overall health of the skin[41].

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