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Understanding Transdermal Patches: A Comprehensive Overview

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ABSTRACT:
Pharmaceutical companies are currently placing significant emphasis on improving drug delivery methods. One innovative approach involves transdermal drug delivery, where a patch is applied to the skin to administer medication. Given that an adult's skin covers an area of 1.5 to 2 m2, it is the body's largest organ by mass. The first transdermal patch approved by the FDA for motion sickness was scopolamine in 1979, followed by nitroglycerine in 1981. These patches penetrate the skin, entering the bloodstream to deliver prescribed dosages. Currently, transdermal patches are used for various purposes, including delivering fentanyl for chronic pain, addressing motion sickness, treating cardiovascular issues, and aiding smoking cessation with nicotine patches. While conventional transdermal patches serve the dual purposes of medication release and storage, they face challenges such as limited release and dosage constraints. The field of transdermal drug delivery has evolved, incorporating technologies like smart patches with built-in sensors to monitor patient conditions and adjust drug delivery accordingly. In 2014, a team of scientists developed a smart patch sensor platform using microneedles for continuous and painless intradermal glucose monitoring in diabetics. Advancements also include personalized transdermal patches tailored to individual patient needs using 3D printing technology. Additionally, researchers are exploring the use of 3D-printed patches to aid in wound healing.

KEYWORDS: Medication patches, Skin administration, Personalized medicine, Chronic pain management, FDA-approved patches.

1. INTRODUCTION

Pharmaceutical corporations are now paying close attention to drug delivery methods. The primary goal of creating alternative medication delivery technologies is to improve drug delivery's effectiveness and safety while giving patients greater convenience[1].

The most common method of medicine delivery is oral. The PH, first-pass metabolism, medication breakdown in the gastrointestinal system due to enzymes, and other issues are some of its drawbacks. Alternatively, injections using hypodermic needles have been employed to administer medications that cannot be taken orally. Nevertheless, there are a number of disadvantages, including discomfort at the injection site, and drug elimination after administration[2].

An innovative medication delivery mechanism was created to overcome these issues. The administration of drugs transdermally is one such method. This approach works by applying a patch to the skin to deliver the medication. With an adult's skin area ranging from 1.5 to 2 m2, the skin is the largest organ in the body in terms of mass. Since the earliest known medical records of mankind, drugs have been administered topically to cure superficial illnesses, to manage systemic ailments through transdermal administration of medicines, and as cosmetics. For example, in ancient Egypt and Babylonian medicine (c. 3000 BC), plant, animal, or mineral extracts were used to make salves, ointments, potions, and even patches. However, it wasn't until the latter part of the 20th century that the routine uses of transdermal delivery systems became widespread, thanks to advancements in delivery technology that made it possible to precisely and consistently provide medication via the skin for systemic effects[3].

Scopolamine was the first transdermal patch for motion sickness that the FDA approved in 1979. 1981 saw the approval of nitro-glycerine as the second patch. There are many transdermal patches on the market these days. Clonidine, testosterone, fentanyl, nicotine, hormones, and so forth, are a few examples. These patches are often worn for one to seven days, depending on the circumstances[4][5].

A transdermal patch is used to penetrate the skin and enter the bloodstream to administer a prescribed dosage. Currently, transdermal administration systems are available for fentanyl for chronic pain, motion sickness, cardiovascular illness, and nicotine for quitting smoking. Transdermal delivery prevents pulsed entry into the systemic circulation, permits continuous input of medications with short biological half-lives, and allows controlled, continuous drug administration. When comparing transdermal drug delivery system, to oral and conventional injection methods, there are numerous benefits[6].

ADVANTAGES

- Avoidance of first-pass metabolism.
- Avoidance of gastro-intestinal incompatibility.
- Predictable and extended duration of action.
- Utilization of drugs with short biological half-life.
- Narrow therapeutic window.
- Improves physiological and pharmacological response.
- Avoiding the fluctuation in drug levels.
- Inter and intra-patient variations.
- Maintains plasma concentration of potent drugs.
- Termination is easy at any point of time.
- Greater patient compliance due to the elimination of multiple dosing profile.
- Ability to deliver drug more selectively to a specific site.
- Provide suitability for self-administration.
- Enhance therapeutic efficacy.

DISADVANTAGES

- The drug must have some physicochemical properties for penetration through stratum corneum.
- The transdermal delivery will be very difficult, if the drug dose required is more than 10mg/kg for their therapeutic application.
- Only relatively potent drugs are suitable candidates for TDDS.

- The barrier function of the skin varies between different sites on the same person, among individuals and with age[7].

2. TYPES OF TRANSDERMAL PATCHES

2.1 Single-layer drug in adhesive: The medication is within the sticky adhesive layer. The medicine is released onto the skin through the adhesive layer, which also acts as glue to hold the several layers together. There is a backing and a temporary line around the sticky layer[8].

2.2 Multi-layer drug in adhesive: This approach is similar to the layer except that it has an instant release layer and a layer for regulated release of the medication in addition to the sticky layer. Because of the sticky coating, the drug is released[9].

2.3 Reservoir: A liquid compartment holding a medication solution or suspension and kept apart from the release liner by an adhesive and semi-permeable membrane define the reservoir transdermal system architecture. The skin adhesive component of the product can be applied in two different ways: either in a concentric pattern surrounding the membrane or as a continuous layer between the membrane and the release liner[10].

2.4 Matrix: A semisolid matrix containing a medication solution or suspension in direct contact with the release liner characterises the design of the matrix system. The skin adhesive component is integrated into an overlay, arranged in a concentric arrangement around the semisolid matrix[10].

2.5 Vapour patch: The adhesive layer in this kind of patch releases vapour in addition to holding the different layers together. The newest products on the market are vapour patches, which release essential oils for as long as six hours. The primary function of the vapour patches for decongestion. They emit essential oils. Controller vapour patches are another type of vapour patch available that enhances the quality of slumber. There are also vapour patches on the market that cut down on how many cigarettes a person smokes in a given month[11][12].

3. COMPONENTS OF TRANSDERMAL PATCHES

3.1 Drug: Only strong medications can be administered transdermally because only those with daily dosages of five to ten milligrams work well this way. Since it offers strong solubility and penetration properties, the medication candidate should have a lower molecular weight, or less than 600 Dalton, and moderate lipophilicity (log P = 1-3). The optimal solubility theory predicts that a medicine with a low melting point will have good solubility. The drug's saturated solution pH should be between 5 and 9, and its melting point should be less than 200°C. A medication's half-life should not exceed ten hours. The medication ought should not cause skin allergies[13][14][15][16][17][18]

3.2 Polymer: The transdermal drug delivery system's basis is reinforced with polymers. The polymer that is utilised must be inert in order to prevent reactions with the excipients or the active substance. It must remain steady and not break down while being stored. The medicine should diffuse at the intended rate due to the polymer's molecular weight and chemical activity. The chosen polymer should not be poisonous and should be biocompatible with skin[13][19][20].

3.3 vehicle : The stability of the vehicle is taken into consideration when choosing a transdermal medication delivery system. It must not change its nature or have a chemical reaction with the medicine. It ought to be hostile or non-toxic to the skin of the host[13][21].

3.4 Penetration enhancer: Accelerants, sorption promoters, and permeation enhancers are other names for penetration enhancers. The stratum corneum's barrier function is necessary for its protective

function, but it may also impede medication transdermal distribution via it. As the primary drug delivery pathway via intracellular channels, the lipid section plays a varied role in the initial absorption process. By using the following mechanism, penetration enhancers can momentarily reduce the skin's barrier function to increase medication flux[13][22][23][24].

3.5 Fluidization of lipid bilayer: It has been shown that penetration enhancers including dimethyl sulfoxide (DMSO), alcohols, and fatty acids change the barrier property of the stratum corneum by loosening or fluidizing its highly organised bilayer structure and so enhance its permeability. They accomplish this by creating permeable pores, or microcavities, in the lipid bilayer, which raises the free volume ratio and, in turn, the drug's diffusion coefficient. In order to increase permeability, these enhancers may also alter the bilayer structure of protein materials [13][24][15].

3.6 Lipid disruption: There are instances where the penetration enhancers mix uniformly and permeate into the lipids. They cause the stratum corneum to become more permeable by creating water channels that disrupt the intracellular lipids[13][25].

3.7 Interaction with keratin: The keratin filaments found in corneocytes can interact with penetration enhancers like DMSO, urea, and surfactants to cause internal cell disruption, which raises the diffusion coefficient and permeability [13].

3.8 Increased partitioning and solubility in stratum corneum: By disturbing the stratum corneum, penetration enhancers such as ethanol and polyethylene glycol (PG) boost solubility within the stratum corneum by shifting the skin's solubility parameter (δ) closer to their solubility parameter. This modifies the partition coefficient by raising the miscibility[13].

The ideal properties of penetration enhancers are:

- It should not be toxic, irritant or allergenic to the skin.
- The activity of the penetration enhancer should be predictable and reproducible.
- It should be inert andnot possess any pharmacological property. Its effect should be unidirectional i.e. they should only allow the drug to pass in while preventing the loss of endogenous material from the skin.
- It should not interact with the drug or other excipients in the system. Penetration enhancers should be compatible with a wide range of excipients and drugs.
- They should be stable, both physically and chemically.
- It should have a rapid effect for a predictable period of time.
- The penetration enhancer used should be economical.

Because permeability enhancers also interfere with viable cell membranes, one typical downside of their efficacy is that they frequently resembles skin discomfort. Whatever these enhancers' manner of action, the effects ought to be transient and reversible[13][22][26][27][28].

3.9 Plasticizer: Depending on the type and concentration of plasticizer, plasticizers can be utilised to increase medication delivery via transdermal systems, enhance film formation, and reduce cracking. Moreover, they raise the polymer's diffusivity by lowering its glass transition temperature. According to reports, plasticizers like sorbitol, glycerine, and PEG can alter the pace at which the therapeutic ingredients in a transdermal medication delivery system release their active ingredients[13][29].

3.10 Backing laminate: The system is held together by the backing layer. It shields the patch from the outside world. It is frequently selected due to its adaptability, look, requirement for occlusion, and imperviousness to medication enhancers and permeability[13].

3.11 Release liner: Before the patch is applied to the skin, the protective liner covering the release liner is removed. The patch is safeguarded while being stored[13][19][30].

3.12 Adhesive: The adhesive is used to adhere the patch's components to the skin. The glue must not be harmful, irritating, or cause skin allergies. It must adhere well to all skin types, including oily, normal, wrinkled, moist, and hairy ones. It ought to offer strong resistance to moisture and humidity. It must be inert and unaffected by medications or other excipients. It should be simple to remove the adhesive without endangering the skin[13][31][32].

4. PREPARATION OF TRANSDERMAL PATCHES

4.1 Circular Teflon mould method: An organic solvent is used to dissolve solutions that include polymers in different ratios. Half as much of the same organic solvent is used to dissolve the calculated amount of medication. The second half of the organic solvent is used to dissolve enhancers at varying concentrations before adding them. A plasticizer is added to the drug-polymer solution, such as Di-N-butyl phthalate. After mixing the entire mixture for 12 hours, pour it into a circular Teflon mould. To regulate solvent vaporisation in a laminar flow hood model with an air speed of 0.5 m/s, the moulds must be set on a flat surface and covered with an inverted funnel. For twenty-four hours, the solvent is left to evaporate. Before evaluation, the dried films must be held for a further twenty-four hours at 25±0.5°C in a desiccator filled with silica gel to prevent ageing effects. These kinds of films have to be reviewed within a week after production. Several bio adhesive polymers, including sodium carboxymethyl cellulose (Na-CMC), hydroxypropyl cellulose (HPC), hydroxypropyl methyl cellulose (HPMC), and Carbopol 934, were used to cast films from organic and aqueous solutions. The physical and mechanical characteristics, swelling behaviours, in-vitro bioadhesion, drug permeation via the bovine buccal mucosa, and in-vitro drug release of the produced films were all examined. It was discovered that these characteristics varied greatly based on the techniques of manufacture, the kind of polymers, and the proportions at which the plasticizer (polyethylene glycol) and film-forming agent (ethyl cellulose and polyvinylpyrolidene) were added. The acquired data showed that for a minimum of six hours, the oral cavity's ketorolac concentration remained above 4.0 µg/mL. This study demonstrated the potential benefits of using ketorolac topically and systemically[33][34].

4.2 Asymmetric TPX membrane method: A heat-sealable polyester film (type 1009, 3m) with a 1cm diameter concave can be used to manufacture a prototype patch. This film will serve as the backing membrane. The drug sample is injected into the concave membrane, sealed with an adhesive, and covered with an asymmetric TPX {poly (4-methyl-1-pentene)} membrane. The dry/wet inversion method is used to create them. To create a polymer solution, TPX is dissolved at 60°C in a mixture of nonsolvent ingredients and a solvent (cyclohexane). Using a gardner knife, the polymer solution is cast to a predetermined thickness on a glass plate after being maintained at 40°C for 24 hours. Following a 30-second evaporation of the casting film at 50°C, the glass plate must be submerged right away in a coagulation bath at a temperature maintained at 25°C. The membrane can be removed after 10 minutes of immersion and air-dried for 12 hours at 50°C in a circulation oven. Studies have shown that asymmetric poly(4-methyl-1-pentene) (TPX) membranes made using the dry/wet inversion method were used to deliver nitro-glycerine (NTG), a medication used to treat angina pectoris, transdermally. Using a Franz cell, the flow of NTG across the TPX membrane was studied in vitro. The findings showed that the membrane structure, which is controllable by adding non-solvents to the casting solution, has a significant influence on the NTG flux through asymmetric TPX membranes. Different types of

membranes with varying NTG-release rates can be created by varying the quantity of non-solvents applied. Additionally, it was discovered that the NTG dissolving rate of a prototype TPX patch, when using an appropriate drug formula, is equivalent to that of a commercial patch called Transderm-Nitro[33][35].

4.3 "IPM membrane" method: The medication is mixed with water and propylene glycol that contains carbomer-940 polymers, and the mixture is agitated for 12 hours using a magnetic stirrer. Triethanolamine is added to the dispersion to neutralise it and make it viscous. If the drug has very poor solubility in an aqueous solution, a solution gel can be created by using a buffer (pH 7.4). The resulting gel will be integrated into the drug-in-adhesive transdermal patch, or IPM (isopropyl myristate) membrane, and its ability to administer anastrozole to specific sites will be assessed, to facilitate the passage of anastrozole through rat skin in vitro, several sticky matrixes, permeation enhancers, and anastrozole concentrations were tested. The formulation comprising DURO-TAK® 87-4098 (pressure-sensitive adhesive), IPM 8%, and anastrozole 8% had the optimum skin penetration profile (in-vitro). Blood, skin, and muscle samples were obtained at various periods after the anastrozole patch was removed from the mouse abdomen skin, in order to conduct investigations on the disposition of tissue locally. Mice were reported to have a high accumulation of the medication in the skin and muscle tissue beneath the patch application site, which was compared to the levels observed following oral administration. These results demonstrated that the use of anastrozole transdermal patches for site-specific drug delivery to achieve a high local drug concentration in the breast tumour location was a suitable delivery method[33][36].

4.4 Mercury substrate method: A plasticizer and polymer solution are added to the medication to dissolve it. In order to create a homogenous dispersion, stir for ten to fifteen minutes. Then, pour the mixture into a mercury surface that has been levelled and cover it with an inverted funnel to control the solvent evaporation of the transdermal matrix type patches of terbutaline sulphate, which were made using ethyl cellulose and cellulose acetate polymer. Solvent casting was used to create the transdermal terbutaline sulphate patches using a mercury substrate. Several polymeric transdermal terbutaline sulphate patches were made for the current study. Studies were conducted to determine how permeability enhancers affected the drug's permeability through cellulose acetate and ethyl cellulose patches. The polymeric mixtures demonstrated good film-forming qualities, and it was discovered that casting on a mercury substrate produced high-quality films. Using mercury as a substrate, Eudragit RL 100, Eudragit RS 100, Polyvinyl pyrollidone (PVP) as polymers, glycerol and propylene glycol as plasticizers, and Span 80 as a permeation enhancer, transdermal patches containing glibenclamide (1.06 % w/v, or 13.5 mg/cm2) were created by solvent casting technique. With 98.02 percent complete and prolonged release, the formulation containing Eudragit RL 100 and propylene glycol as plasticizers performed well[33].

4.5 "EVAC membrane" method: Rate control membranes such as polyethylene (PE), ethylene vinyl acetate copolymer (EVAC) membranes, and 1% Carbopol reservoir gel can be utilised to prepare the target transdermal treatment system. The gel is made with propylene glycol if the medication is not soluble in water. Propylene glycol is used to dissolve the drug; Carbopol resin is then added to the mixture and neutralised with a 5% w/w sodium hydroxide solution. The medication (in gel form) is applied to a backing layer sheet that covers the designated area. To create a leak-proof device, a rate-regulating membrane will be placed over the gel, and the borders will be sealed with heat.Rabbits were used to test the irritation of transdermal devices that delivered levonorgestrel and the penetration

enhancer ethyl acetate, either with or without ethanol. After the 24-hour delivery system was applied, erythema and edema were evaluated 24, 48, 72, and 7 days later. It was discovered that the devices caused mild to moderate irritation, with erythema being the main symptom. Using either pure ethyl acetate or ethyl acetate-ethanol (7:3 v/v) as enhancers, no changes were seen between the devices. Devices that used pure ethanol as an enhancer produced irritation levels comparable to those that used pure ethyl acetate or ethyl acetate ethanol[33][37].

4.6 Aluminium-backed adhesive method: If the loading dose for a transdermal drug delivery system is more than 10 mg, unstable matrices may be produced. The adhesive film approach with aluminium backing is appropriate. Since the majority of medications and adhesives are soluble in chloroform, it is the solvent of choice for preparing the same. Adhesive substancesare added to the drug solution and dissolved in chloroform, once the drug is dissolved. Aluminium foil is used to line a specially constructed aluminium former, and cork blocks that fit firmly are used to blank off the ends. Utilising the polymers Eudragit E 100 (EE 100) and polyvinyl pyrrolidone VA 64 (PVP VA 64), developed medicated films (containing Losartan Potassium - LP) were made in a film casting assembly with aluminium foil. The system was intended to be designed in a way that would allow for the regulated distribution of LP across intact skin in order to produce an anti-hypertensive effect that would last longer. The films were assessed for their physical characteristics, pharmacodynamics, in-vitro skin penetration, and in-vitro drug release investigations. With a high drug concentration (>99%), the physical parameters were found to be quite excellent. Wistar albino rats were used in the pharmacodynamic experiments, which were conducted using the tail-cuff method. Methyl prednisolone acetate was used subcutaneously for two weeks to induce hypertension. The blood pressure was found to be considerably ($P < 0.001$) lower after applying the created matrix patch, and this effect persisted for 24 hours. Primaquine's ability to permeate the entire thickness of human skin removed two acrylate transdermal adhesives. The National Starch 387-2516 and 387-2287 were combined to create a primaquine base that resulted in 1-cm-diameter patches with an aluminium foil backing and 10 mg of medication per patch. In Franz-type diffusion cells, the patches were placed on cadaver skin, and over a day, the amount of primaquine that permeated the skin was measured. Quite high fluxes were discovered[33][38].

4.7 Free flim method: Casting on a mercury surface creates a free film of cellulose acetate. An organic solvent, like chloroform, is used to prepare a polymer solution, such as 2% w/w. The polymer solution is mixed with the plasticizer at the ideal concentration (for example, 40% w/w of polymer weight). A glass ring that is placed over the mercury surface in a glass petri dish is filled with a small volume (5 ml) of polymer solution. An inverted funnel placed above the petri dish regulates the solvent's rate of evaporation. After the solvent has completely evaporated, the mercury surface is examined to detect the creation of a layer. Before being used, the dried film is removed and kept in a desiccator between the wax paper sheets. The volume of the polymer solution can be adjusted to create free films with varying thicknesses. The metformin hydrochloride transdermal medication administration method,was developed using the solvent evaporation process, it was made with mixtures of the hydrophilic polymer polyvinyl pyrrolidone and the hydrophobic polymer ethyl cellulose in various ratios (e.g., 1:2, 1:4, 1:6, 1:8, 2:1, 4:1, 6:1 and 8:1 w/w). Dibutyl phthalate was utilised as a plasticizer, while polyvinyl alcohol was utilised to create the backing membrane. A number of physiochemical characteristics, including film thickness, tensile strength, moisture content, moisture uptake, and water vapour transmission rate, were assessed for the produced polymeric films. Patch permeability tests were conducted using a Keshary-

Chien diffusion cell on rat abdomen skin and commercial semi-permeable membranes. Within 24 hours, the patch with the optimised formulation showed good drug release (e.g., 96.92%). created celecoxib-containing transdermal patches to treat osteoarthritis. The method was developed using varying ratios of ethyl cellulose to polyvinyl pyrrolidone (EC/PVP). When the percentage of PVP added to the formulations increased, the release rates and flow rose linearly. Studies conducted in vitro revealed improved performance when an enhancer (5% v/v oleic acid) was present. It was discovered that the total quantity of medication that permeated was proportionate to the square root of time. Rats' paw edema was 100% inhibited by the optimised formulation (anti-inflammatory action) for a maximum of six hours. The rat hind paw edema technique caused by carrageenan (1% w/v) was used to study the anti-inflammatory impact in vivo[33].

5. FACTORS AFFECTING DRUG PERMEATION THROUGH THE SKIN

5.1 ph: The internal environment has a nearly neutral pH range of 7-9, but the skin's pH typically ranges from 4 to 6. It was once believed that an acidic pH served as a defence mechanism against microorganisms. It has also been shown recently to support the efficient operation of the enzymes responsible for the production and upkeep of skin. The pH level of the skin is a result of the stratum corneum's water-soluble components, sebum and sweat secretions, and carbon dioxide elimination. Skin pH controls the permeability barrier and maintains the cohesiveness and integrity of the stratum corneum. The amount of unionised medication that is available for absorption through percutaneous penetration can be impacted by the skin's pH. The pH-partition hypothesis states that only the drug's unionised form has a considerable chance of passing through the lipid barrier. Formulation with extremely high or low pH value may damage skin[13][39][40][41][42].

5.2 Temperature: Theoretically, there should be a positive correlation between the drug's percutaneous penetration and the temperature of the skin. In warmer temperatures, the skin is more porous. It has been found that heat increases the kinetic energy of the drug molecule as well as the lipids, proteins, and carbohydrates in the cell membrane. This can leadto a decrease in local drug delivery but an increase in drug transport to the dermis. Research has indicated that alterations in the permeability of the cell membrane require a temperature shift of roughly 5°C[13][43][44].

5.3 Molecular weight: The drug's molecular weight has an inverse relationship with the rate of percutaneous absorption. It might have an impact on the drug's diffusion coefficient. Less than 500 Dalton is the ideal molecular weight for transdermal drug delivery systems that use passive diffusion; however, the rate of penetration can be accelerated by using different penetration enhancers[13][21].

5.4 Partition coefficient: To identify how a medicine is distributed within an organism in order for it to exert its biological activity, log P, also known as the partition coefficient, is crucial. When administered topically, hydrophilic medications have low absorption because they partition poorly through the stratum corneum's lipid matrix. Drug absorption is quickly cleared by cutaneous blood flow, which could lead to low tissue levels[13][45].

5.5 Biotransformation of drug in skin: There is a wealth of data supporting the existence of enzymes in the skin, particularly CYP family enzymes, which may facilitate the biotransformation of drugs that penetrate the cutaneous environment. This biotransformation could increase the drug's bioavailability or work in concert to change a prodrug into an active metabolite. However, it is important to remember that this cutaneous first-pass or biotransformation is smaller than what is seen in the liver[13][46].

5.6 Cutaneous microcirculation: Increased tissue perfusion resulting from improved medication absorption is contingent upon several factors, including the structure of the skin's vascular plexuses. Two plexuses of arterioles-an upper horizontal plexus situated in the papillary dermis immediately beneath the epidermis and a lower horizontal plexus situated in the deep dermis at the edge of the subcutaneous tissue beneath it-have been identified as the sites of cutaneous microcirculation organisation. Different capillary networks arise from each plexus of arterioles[13][47].

5.7 Hydration: Hydrating the stratum corneum increases the penetration rate of most medicines. By doing this, it increases the drug's bioavailability by breaking up the stratum corneum's compacted horny layer structure. Because impermeable films stop the skin's surface from losing water, the stratum corneum becomes more hydrated, shortening the diffusional path. The concentration gradient across the skin, the stratum corneum's partitioning and transport, and the skin's level of moisture all affect the flux through it[13][48][49][50].

5.8 Age: Statistics show that despite the thickness and number of cells in the cellular epidermis has reduced, the number of stratum corneum cell layers has only marginally grown, particularly in males. Age affects the pH of the skin's surface. As we age, our skin contains more unbound water molecules that aren't connected to proteins. This could slow down the percutaneous penetration of drugs, especially those that are hydrophilic. More over as people age, their levels of key lipids, particularly ceramides, likewise decline[13][51][52][53].

5.9 Gender: Studies show that there is statistically no change in the stratum corneum's thickness or number of cell layers. Despite the discovery that men's cellular epidermis is thicker than that of women's[13][54].

5.10 Body site: According to the studies conducted, the smallest number of cells in the stratum corneum was found to be in genital areas, and the largest number of cells was in the heels [13][51].

5.11 Sun exposure: The stratum corneum is thicker in the sun exposed areas compared to the thinner stratum corneum in the sun-protected area[13][55].

5.12 Blood flow: The absorption of drug may be limited by the blood flow through the dermis. For example, if a drug with vasoconstriction activity is given through any other route, it will significantly impair the blood flow through the skin and thus affect drug clearance for the transdermal drug delivery system[13][49].

5.13 Skin condition: In atopic dermatitis, the stratum corneum is less able to bind water, so the skin of AD patients is dry and inelastic. The changed composition of intercellular lipids with increased cholesterol levels and reduced level of ceramides significantly contribute to the reduction of barrier function. The pH of the skin is also increased as compared to healthy skin[13][56].

6. EVALUATION PARAMETERS

6.1 Physical appearance: The prepared patches were physically examined for colour, clarity and surface texture [4][57].

6.2 Interaction studies: An integral component of any formulation is the excipients. At several phases of the manufacturing process, interaction studies are carried out to verify that there is no chemical reaction between the medications and the formulation's excipients. Studies are conducted using a variety of methods.

- UV spectroscopy
- Thermal analysis

- FT-IR spectroscopy
- Chromatographic techniques[58]

6.3 weight uniformity: Before the test, the prepared patches are dried at 60 degrees Celsius for four hours. A precise portion of a given size is taken from different areas of the patch and balanced. Next, the standard values and average weight are computed[59].

6.4 Thickness of patch: Using a digital micrometer, the thickness of the drug-loaded patch is measured at several locations. From the individual results, the average thickness and standard deviation are calculated[4][60].

6.5 Percentage of moisture content: Each medication-loaded patch is weighed separately and stored for a full day at room temperature in a desiccator filled with fused calcium chloride. The films are reweighed a day later. Using the formula shown below, find the moisture content.

Percentage moisture content = (initial weight – final weight) *100/ final weight[4][60].

6.6 Drug content: A designated patch area needs to be dissolved in an appropriate volumetric flask. After that, the mixture is filtered using an appropriate technique and a filter medium[4][61].

6.7 Thumb back test: It is a qualitative test to evaluate the tack property determination of adhesive. The thumb is simply placed on the adhesive, and the relative tack property is detected[4][62].

6.8 Skin irritation studies: Both human volunteers and animals are used in this experiment. To proceed with the test, the necessary clearances and permissions from several regulatory boards are required. The animal must be pretreated to remove the hair. After a full day, the patch is to be taken off, the skin examined, and the degree of the skin injury is to be graded into five categories[63].

6.9 Stability studies: In accordance with the ICH standards, stability tests must be carried out by keeping the TDDS samples for six months at 40±0.5°C and 75±5% relative humidity. The samples were taken out at0,30,60,90, and 180 days, and their drug content was appropriately analysed[63].

6.10 Flatness test: To find out how smooth the film is, a flatness test is run. Three film strips—two from each of the film's sides and one from the centre-need to be cut and measured in length. The length variation is expressed as a percentage of constriction. 100% flatness is said to be equal to 0% constriction[4][58][61].

6.11 Water vapour transmission rate: Transmission cells for this investigation were equal-diameter vials. After a thorough cleaning, these cells were dried in an oven. The polymeric patches, each measuring one centimeter in area, were adhered to the brim of the cells using an adhesive after adding around one gramme of fused calcium chloride. After precisely weighing and recording the starting weight of the cells, they were stored in closed desiccators with a saturated potassium chloride solution to maintain a RH of 80–90%. After a day, the cells were removed and weighed. The formula was used to determine the amount and rate of water vapour transported based on the weight differential. The standard way to express the water vapour transmission rate is as grammes of moisture gained/(g/hr.cm2)[4][58][62].

TRANSMISSION RATE = (FINALWEIGHT – INITIAL WEIGHT)/ TIME ×AREA × 100

6.12 Shear adhesion test: The purpose of this test is to determine an adhesive polymer's cohesive strength. A stainless-steel plate is covered with adhesive-coated tape, and to cause the tape to pull in a direction parallel to the plate, a predetermined weight is suspended from it. The time taken to remove the tape from the plate is used to calculate shear adhesion strength. Greater shear strength results from longer removal times[4][62][61][59][63].

6.13 Peel adhesion test: Peel-adhesion is the term used in this test to describe the force needed to remove an adhesive covering from a test substrate. The variables that affected the peel adhesion properties were the adhesive polymer's molecular weight and the kind and quantity of additives. A single piece of tape is applied to a backing membrane or stainless-steel plate. It is then pulled away from the substrate at a 180-degree angle, and the force needed to remove the tape is calculated. The amount of effort needed to remove an adhesive covering from a test substrate is known as peel adhesion. The adhesive should allow the gadget to make sufficient contact with the skin and should not harm the skin when removed. For transdermal devices, it is ideal to have no residue on the substrate as this signifies "adhesive failure". The presence of remnants on the substrate indicates "cohesive failure," which denoting, coating deficiency in cohesive strength[4].

6.14 Rolling ball tack test: In this test, a 7/16-inch-diameter steel ball is rolled down an inclined surface with a horizontally positioned patch facing the upward sticky surface. On the patch, the ball rolls down and travels a distance horizontally. The tack quality adhesive patch's can be determined by measuring the ball's run- length[4].

6.15 Quick stick (peel tack) test: In this test, the tape is pulled at a speed of 12 inches per minute at 90°C away from the substrate. The tack value, which is given in ounces or grammes per inch of width, is a measurement and record of the peel force needed to break the binding between adhesive and substrate[4].

6.16 Uniformity of dosage unit test: To fully extract the drug from the patch, chop up a precisely weighed portion of the patch, transfer it to a volumetric flask of a specified capacity, dissolve it in an appropriate solvent, sonicate the mixture, and add more medication as needed. After letting the resultant solution to settle for about an hour, the supernatant was appropriately diluted with the proper solvent to achieve the required concentration. The solution was passed through a 0.2mm membrane filter before being subjected to an appropriate analytical technique (UV or HPLC) to determine the drug concentration per piece[4].

6.17 Probe tack test: This test involves touching the adhesive with the tip of a clean probe that has a predetermined surface roughness to see if a bond forms between the probe and the adhesive. It breaks mechanically when the probe is removed later. Tack is the unit of measurement for the force needed to remove the probe from the adhesive at a set pace. It is represented in grammes.

6.18 Tensile strength: A 40 by 15 mm little film strip was utilised. To provide support for the film when it was inserted into the film holder, one end of the strip was secured between adhesive tapes. In order to maintain the strip's straightness during stretching, a tiny pin was positioned between the adhesive tapes at the other end of the film. The adhesive tape had a little hole created in it next to the pin where the hook was placed. To hold the weights, a small pin was fastened to the opposite end of a thread that was tied to the hook and passed over the pulley. The thread that passes over the graph paper fixed to the base plate has a tiny pointer connected to it. A pulley system was used to pull the film in order to measure its tensile strength. The pulling force of the pan was increased by progressively adding weights until the film broke. Break force was defined as the weight needed to break the film[1][64].

6.19 Solubility studies: In order to conduct the solubility investigations, excess medication was added to each instance and the phosphate buffer flasks holding the excess drug were kept on a water bath shaker NSW-133 (REMI Equipment, Mumbai, India) for a full day at 328°C. Following 24-hour period, spectrophotometric analysis of the solutions was conducted at 275 nm, the previously reported absorption maxima, and drug concentrations were computed[1][65].

6.20 Determination of partition coefficient of drug: Phosphate buffer, pH 7.4, was used as the aqueous phase and n-octanol as the oil phase in the partition coefficient investigation. Equal amounts of the two phases were combined, and they were soaked for 24 hours at 328°C on a mechanical water bath shaker (NSW-133). On a REMI R-23 centrifuge, the saturated phases were separated by centrifugation at 2000 rpm. Standard drug plots were made using octanol and phosphate buffer. 100 mg of the weighed medication was introduced to each of the two phases' equal volumes (10 mL each) in hexaplicate conical flasks. For six hours at 328°C, the flasks were shaken at 100 rpm to achieve full partitioning. Centrifugation was used to separate the two phases for five minutes at 1000 rpm. The contents of each phase were then measured for drugs. With the following formula, the drug Ko/w partition coefficient was determined[1][66].

6.21 Invitro drug release studies: For this test, a Franz diffusion cell was used. Phosphate buffer was the dissolving medium that was employed. Samples were taken out while sink conditions were maintained, and the drug content was assessed using the appropriate analytical methods. Two aspects of dosage forms that are crucial in explaining the drug dissolution profile of controlled release dosage forms are drug release mechanisms and kinetics. A six-spindle Chinese Pharmacopoeia apparatus with glass jars holding 900 ml of phosphate buffer (pH 7.4) and a paddle speed of 50 r/min was used to conduct the dissolution test. Using a glass rod for centering, the patch assembly was carefully positioned at the bottom of the vessel. After being lowered, the paddles were raised 2.5 cm above the patches. The device was calibrated to measure skin surface temperature, which is 32 ± 0.5°C. Five millilitre samples were taken at predetermined intervals for up to ten hours. After that, an equivalent volume of new medium was added, and HPLC was used to determine the drug content. These models are fitted with the dissolution data, and the best match is found to explain the drug's release mechanism[1].

There are various methods available for the determination of the drug release rate of TDDS.

1. **The paddle over disc:**(USP equipment 5) With the exception of the transdermal system being coupled to a disc or cell that is sitting at the bottom of the vessel containing medium at 32 ±5°C, this approach is identical to the USP paddle dissolving apparatus.
2. **The cylinder modified usp basket:**(USP equipment 6) This technique is comparable to the USP basket type dissolution apparatus, with the exception that a hollow cylinder submerged in the medium at 32 ±5°C has the system attached to its surface.
3. **The reciprocating disc:(**USP equipment 7) This technique oscillates patches attached to holders in tiny quantities of media, making the device effective for drug delivery systems with low concentrations. The Paddle over-extraction cell technique is another option.
4. **Diffusion cells:** e.g. franz diffusion cells and its modification,keshary-chien cell:This procedure involves inserting a transdermal device between the diffusion cell's donor and receptor compartments. The receptor compartment, or receptor fluid, or buffer, is facing the transdermal system. Both temperature and agitation speed are maintained constant. Throughout the experiment, magnetic beads are used to continuously agitate the solution in the receiver compartment while the entire assembly is kept on a magnetic stirrer. The receptor fluid is extracted for analysis at prearranged intervals and replaced with an equivalent volume of brand-new receptor fluid. Spectrophotometric analysis is used to determine the drug's concentration[1].

7. RECENT ADVANCEMENT IN TRANSDERMAL PATCHES

There are just two uses for conventional transdermal patches: medication release and storage. While

there are several benefits to this approach, traditional patching has numerous difficulties and disadvantages, such as low release or restricted dosage. Transdermal medication delivery has seen a number of advancements to date. Among these include the creation of innovative patches with improved drug penetration and release, increased loading, and precise drug sensing and release capabilities. All things considered, transdermal medication distribution is a burgeoning field of study and innovation, with a plethora of fascinating new advancements pending.

7.1 Smart Patches: Sensors and other technologies are built into smart patches so that they can monitor patient conditions and modify drug delivery as necessary. A team of scientists created a smart patch sensor platform in 2014 that uses microneedles to provide with continuous, painless intradermal glucose monitoring for diabetics. This patch works by immobilising the glucose-specific c-enzyme glucose oxidase (GOx) and acting as an electrical mediator for glucose detection using a conducting polymer, such as poly (3,4-ethylenedioxythiophene) (PEDOT). Subsequent investigation and advancement led to the creation of an intelligent insulin-releasing patch with 121 nanoparticle-containing microneedles. The patch enters the interstitial fluid between subcutaneous skin cells painlessly. Insulin and the glucose-sensing enzyme glucose oxidase, which changes glucose into gluconate, are both found in the nanoparticles that make up each needle. Polymers that respond to hypoxia envelop these molecules. As demonstrated in, increasing glucose oxidase activity in response to increased glucose creates an oxygen deprived environment within the nanoparticles, which is recognised by the hypoxia-responsive polymer, initiating nanoparticle disintegration and insulin release. The regenerative process of wound healing is intricate and dynamic, with physical and chemical characteristics that are constantly shifting. Its monitoring and care are very beneficial, particularly for patients who are bedridden. A low-cost, flexible, completely printed smart patch that may be applied to the skin to monitor changes in wound pH and fluid volume was described by Iversen et al. Wound dressings can also be made simplywith such bendable sensors. For measuring pH and humidity, the sensor is made up of different electrodes printed on a polydimethylsiloxane (PDMS) substrate. The resulting sensor patch is sensitive to the pH of the wound at a rate of 7.1 ohm/pH. The water content of the semi-porous surface can be measured by measuring the change in resistivity, according to the results obtained by the hydration sensor. In addition to healing wounds, scientists have created a smart patch that can be used to treat and monitor diabetic foot ulcers. Conductive hydrogel patches with an ultra-high transparency polymer network are used to construct this system. Significantly, very transparent conductive hydrogel patches can visually track the progress of wound healing, enhance vascularity, enhance cell-to-cell communication, enhance haemostasis, and prevent wound infection. It successfully encourages the healing of Device FlimwareUpdate by fostering angiogenesis. The adaptable intelligent patch can also promptly detect movements of different body partsand perform indirect blood glucose monitoring by measuring the amount of glucose present in wounds. It's interesting to note that this smart patch can both cure wounds and monitor chronic wound dressings. Additionally, curcumin and other natural substances are delivered via smart patches. Paraffin wax and polypropylene glycol, a phase-change material (PCM), make up the substance. PCM was mixed with heating elements made of graphene, which were produced by laser-scribing polyimide films. With this setup, smart patches with electronically controlled release and repeatable dosages are given a new lease on life. Instead of relying on passive diffusion, the PCM is heated under carefully controlled conditions to start and stop emission, and penetration occurs only when the PCM transforms from a solid to a liquid state. The results showed that the curcumin delivery yields were acceptable and good[67][68][69][70][71][72].

7.2 Dissolving/Degradable Patches: These patches are designed to dissolve into the skin, so there's no need to remove and dispose of them. Frequently made of biodegradable materials, these patches are absorbed by the body after use. In a 2019 proof-of-concept study, researchers successfully administered the antibiotic gentamicin to a mouse model of bacterial infection using a dissolving patch. The results showed that applying a gentamicin-dissolving microarray patch to mouse ears could effectively manage Klebsiella pneumoniae infection. In addition, mice that received lysing patches had less germs in their lymphoid tissue that connected to their noses and in their lungs than did the untreated control group. Dissolving microneedles can be an extremely effective way to provide medications and immunisations that the body is not able to properly absorb (MNs). By localising insulin to the needle utilising a two-step injection and centrifugation process, effective transdermal insulin delivery was achieved. The relative pharmacological availability (RPA) and relative bioavailability (RBA) of insulin derived from MN patches were 95.6% and 85.7%, respectively. This study demonstrates that the use of dissolving patches for insulin delivery yields a respectable relative bioavailability (RBA) when compared to standard subcutaneous injection, showing the effectiveness of dissolving patches in the management of diabetes. On the other hand, scientists have developed a biodegradable microneedle patch that delivers hyaluronic acid (HA) antigen-peptide conjugates for the purpose of cancer immunotherapy prevention. HA-loaded biodegradable HA microneedle (MN) patches are connected to a cytotoxic T-cell epitope peptide (SI-INFEKL) in order to deliver antigens to the skin's immune system efficiently. Interestingly, a single transdermal vaccination with an MN patch expressing the HA-SIINFEKL compound significantly increased tumour growth in B16 melanoma model mice by increasing antigen-specific cytotoxic T-cells. A different group of researchers developed a hypotensive biodegradable patch for transdermal administration of sodium nitroprusside (SNP) and sodium thiosulfate (ST) [81]. Soluble microneedles containing SNPs and STs were produced via centrifugal casting. This method allowed for the steady delivery of SNPs onto microneedles and their immediate release into the bloodstream. Fast and considerable blood pressure reduction was observed with antihypertensive microneedle treatment (aH-MN). It met the clinical requirements for blood pressure control in emergencies involving hypertension. Consecutive ST treatment effectively mitigated deleterious consequences (such organ damage) resulting from continuous SNP ingestion. This study demonstrated an efficient and user-friendly biodegradable patch for treating hypertension. Transdermal patches are also widely used in the cosmetics industry. The non-biodegradable polymers used in cosmetic patches, however, raise concerns because inappropriate disposal in open areas could result in environmental damage. One study suggested using biodegradable polylactic acid (PLA) because it is non-toxic. The PLA/phycocyanin-alginate composite, which was created using a phycocyanin/alginate ratio of 40/60 at 20 °C for 20 hours, has the best qualities in terms of film flexibility and release. Overall, the results are encouraging, but further in vivo or clinical research is required to make significant progress[73][74].

7.3 Three-dimensional 3d printed patches: Researchers are creating transdermal patches that are personalised to each patient's unique demands through the use of 3D printing technology. The usage of a 3D-printed patch to aid with wound healing is one excellent example. Gelatin methacrylate, or GelMA, was investigated as a potential solution with adjustable physical characteristics in a study by Jang et al. GelMA hydrogel including a vascular endothelial growth factor (VEGF)-mimicking peptide was successfully produced utilising a 3D bio-printer owing to the shear-thinning capabilities of hydrogel inks. The hydrogel patch's three-dimensional structure was very porous and capable of absorbing water. It is possible to employ the 3D Gel-MA-VEGF hydrogel patch as a wound dressing because the VEGF

peptide, which is gradually released from the patches, can encourage cell survival, proliferation, and the creation of tubular structures. Transdermal patches, on the other hand, were designed and made using a three-dimensional (3D) printing method known as continuous liquid interface production (CLIP). When compared to the smooth square pyramid shape, the multifunctional microneedle design increased surface area, which improved the surface coating of the model vaccine components (ovalbumin and CpG). The study evaluated in vivo charge retention and bioavailability in mice as a function of the delivery route using fluorescent tags and live animal imaging. Transdermal administration of soluble components produced better skin charge retention than subcutaneous bolus injection, and it also increased the activation of immune cells in draining lymph nodes. Furthermore, the administered vaccination produced dose sparing due to a robust humoral immune response with increased total IgG (immunoglobulin G) and a more balanced IgG1/IgG2a repertoire. Additionally, it triggered a T-cell response that was demonstrated by Th1 (T helper type 1) cytokine-secreting CD4+ T-cells and functionally lethal CD8+ T-cells. To put it briefly, CLIP 3D-printed microneedles coated with vaccine ingredients offer a practical platform for self-administered, non-invasive immunisation. Using a class I resin that was exclusive to them, another team of researchers used stereolithography (SLA) technology to design and print the patch. They demonstrated the potential of these patches for transdermal administration of antibiotics with high molecular weights, such as rifampicin (M(w) 822.94 g/mol). This medication has significant hepatotoxicity, decreased bioavailability, and stomach chemical instability. To improve the mechanical strength and integrity of the patch array, the patch was built with sub-apical holes located in one-quarter of the needle tip. To assess print quality and uniformity across the array, optical and electron microscopy were used to characterise the tips. Additionally, the system was mechanically characterised for penetration and failure analysis. The ex vivo penetration and subsequent transport of rifampicin through the swine epidermis were methodically assessed by the authors. Furthermore, an in vivo investigation using a 3D-printed patch to administer rifampicin showed effective penetration and acceptable bioavailability. Since powder extrusion (DPE) may directly handle medications and excipients in a single step, it has become the most practical method. The goal of the study was to ascertain whether various grades of ethylene-vinyl acetate (EVA) copolymers could be utilised as novel raw materials in transdermal patch manufacturing. The selection of two distinct model medications, namely ibuprofen and diclofenac sodium, was made to examine the potential adaptability of this EVA excipient in the production of patches intended for customised transdermal therapy. Each model medication was mixed with 30% (w/w) EVA. The effective incorporation of the starting material into the final formulation was confirmed by Fourier transform infrared (FT-IR) spectra. Thermal analysis also revealed that the raw polymer's crystalline morphology was altered during the extrusion process, resulting in increased crystallisation at smaller thicknesses. According to this study, direct powder extrusion and EVA technologies could be useful for creating transdermal patches. Drugs with varied melting points can be printed while retaining thermal stability if an EVA type with the right amount of VA is selected. Moreover, it is possible to obtain the required medication release and penetration characteristics. This is, in reality, a significant benefit when considering personalised medication. Acetyl-hexapeptide 3 (AHP-3) can be delivered with 3D printed, customised patches that fit the surface of the skin, according to research by Lim et al. However, creating drug-loaded delivery systems is not a good use for commercially available photocurable resins for 3D printing. This study used two liquid monomers, vinylpyrrolidone (VP) and polyethylene glycol diacrylate (PEGDA), in varying ratios to increase the final polymer's swelling rate, mechanical strength, and polymerization rate. AHP-3

remained stable throughout the production process and had no effect on the physical qualities of the final polymer, according to optimal drug loading on the resin. A customised patch was created in CAD (computer-aided design) software using a 3D scanned facial model, and it was printed in optimised resin using a digital light processing (DLP) 3D printer. The transdermal patches were characterised in vitro and demonstrated penetration of human cadaver skin, as well as their capacity to withstand compression. Human dermal fibroblasts were also only slightly cytotoxically affected by the final polymer. This is the first study to show customised patches created with photopolymers, and it could be a cutting-edge way to enhance medication transdermal administration for efficient wrinkle management[75][76][77][78][79][80].

7.4 High loading/release patches: High drug loading and regulated drug release are necessary for long-acting transdermal medication administration. This innovative pressure-sensitive adhesive (PSA) was modified with hydroxyphenyl (HP) to improve drug-polymer miscibility and enable regulated drug release. The findings demonstrate that, in contrast to ionic and neutral Hydrogen bonds, the dual-ionic H-bonds between R (3)N and R (2) NH-type medications and HP-PSA are reversible and reasonably strong. As a result, patches were able to regulate the medication release rate from 1/5 to 1/2 and dramatically increase the drug loading from 1.5 to 7 times without altering the release profile overall. The HP-PSA-based high-load patch has the potential to deliver drugs for a long time since, according to pharmacokinetic data, it prevented abrupt release, raised the area under the concentration-time curve (AUC), and extended the average dwell time by more than six times. Its mechanical and safety requirements are also satisfied. Mechanistic investigations have demonstrated that relatively strong contacts can also govern drug release, and that repulsion of ionic pharmaceuticals in HP-PSA promotes drug loading. Its reversibility was evaluated through incomplete hydrogen bond transfer, which made the medication release percentage comparable to that of non-functional PSA. In summary, the development of long-acting transdermal drug delivery systems will be aided by HP-PSA's unique interactions, high drug loading efficiency, and regulated drug release capabilities. Furthermore, the synthesis of double-ionic H-bonds offers further motivation for diverse drug delivery schemes in non-polar settings. Pharmaceutical polymers are commonly employed to restrict drug recrystallization through strong intermolecular hydrogen and ionic bonding, albeit at the expense of drug release rates in transdermal patches. Researchers devised a novel drug approach using IL (ionic liquid) to boost drug loading in order to overcome this problem. The model polymer selected was a pressure-sensitive adhesive (PSA) based on carboxyl. The PSA medication load increased five times, according to the results. The drug's and PSA's carbonyl groups generated strong ionic and normal hydrogen connections, which worked in concert to cause this. This work offered a potent tool for the creation of high-drug load, high-release patches and revealed a completely novel mode of action. In a different investigation, the same team of researchers used COOH polyacrylate polymer (PA-1) to create a high-capacity, high-release transdermal patch that would administer NSAIDs, specifically ibuprofen. PA-1's epidermal absorption and drug load were increased by 2.5 and 2.4 times, respectively. Repulsive interactions weaken the hydrogen bond that forms between the drug (COOH) and PA-1 (COOH), while dielectric spectroscopy, electron paramagnetic resonance (EPR) spectra, the four-point probe method, and molecular modelling with the appearance of COO-all confirmed PA-1's enhanced conductivity. In conclusion, these findings demonstrated that ion-ion repulsion through the reduction of hydrogen bonding can be a practical approach for creating high-emission, large-capacity patches [81][82][83].

8. CONCLUSION

Transdermal drug delivery is a promising alternative to traditional methods like oral and injectable routes, offering increased efficiency, safety, and patient convenience. This method involves administering medications through skin patches, with historical roots dating back to ancient medical practices. The first transdermal patch was approved in 1979, leading to subsequent advancements in the field. Today, various transdermal patches, such as Clonidine and Fentanyl, demonstrate the versatility and effectiveness of this drug delivery system. These patches offer controlled and continuous drug release, particularly beneficial for medications with short biological half-lives. Transdermal drug delivery addresses challenges like first-pass metabolism, enzymatic degradation in the gastrointestinal tract, and discomfort associated with hypodermic needle injections. The elimination of pulsed entry into the systemic circulation contributes to a more stable and predictable therapeutic effect. As pharmaceutical companies continue to invest in and refine transdermal drug delivery technologies, the future holds promise for further advancements and expanded therapeutic applications.

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Conflict of Interest

Authors declare that no conflicts of interests.

Ethical Approval

This article does not contain any human participant and animal work.

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