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A Review on Transdermal Patch and Its Importance in Drug Delivary System

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ABSTRACT
To address the challenges associated with oral drug delivery, a transdermal drug delivery system was developed. To deliver a specific dosage of medication through the skin and into the bloodstream, a transdermal patch is an adhesive patch that has been medicated and applied to the skin. This frequently encourages a body part that has been injured to heal. The capacity to regulate medicine to a understanding in a controlled way by means of a transdermal fix is one advantage over other strategies, such as verbal, topical, intravenous, intramuscular, etc. Typically, this is achieved by either a porous membrane enclosing a drug reservoir or by body heat melting thin layers of medication embedded in the adhesive. As a result, only drugs whose molecules are small enough to pass through the skin can be administered via transdermal delivery systems. This is the main drawback of these systems. The preparation processes for several transdermal patch types, including matrix patches, reservoir types, membrane matrices, drug-in-adhesive patches, and micro-reservant patches, are covered in this review article. Furthermore, reviewed have been the numerous techniques for assessing transdermal dosage forms.

KEYWORDS: Transdermal Patch, Matrix Patches, Reservoir Type, Membrane Matrix, Drug-In-Adhesive Patches, Micro Reservoir Patches

I. INTRODUCTION:

Through the skin and into the bloodstream, a transdermal patch administers a predetermined dosage of medication. The FDA initially authorised transdermal patch products in 1981. At the moment, transdermal delivery systems that contain fentanyl for chronic pain, clonidine and nitro glycerine for cardiovascular disease, scopolamine (hyoscine) for motion sickness, and nicotine to help with quitting smoking are available. In addition to allowing continuous input of medications with short biological half-lives and preventing pulsed entry into the systemic circulation, transdermal delivery offers controlled, continuous drug administration. Compared to traditional injection and oral techniques, TDDS has numerous advantages. It lessens the strain on the liver and digestive system that the oral route frequently causes. It avoids negative drug side effects from transient overdoses and improves patient compliance. Particularly for patches that call for a single weekly application, it is very convenient. A straightforward dosage schedule likethis promotes patient adherence to medication treatment.

AIM AND OBJECTIVES

AIM
To describe the Methods for Enhancing Transdermal Drug Delivery

OBJECTIVE
1. To learn more about transdermal patch types from revive.
2. Analyse the drug's physiochemical characteristics
3. To talk about the parameters of the evaluation.
4. To talk about transdermal patches promising future

Literature Review

- According to Aggarwal G, Dhawan S, et al. using the prodrug method, medications with unfavourable partition coefficients can be delivered more effectively through the skin and transdermally. A moiety is included as part of the prodrug design in order to improve the parent drug's solubility and transport in the stratum corneum, as well as to raise the partition coefficient. Esters enhance a drug's solubility in the aqueous epidermis by hydrolysing it once it reaches the viable

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epidermis.

- According to Heather AE et al. Testing is done

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four hours at 60°C. To weigh in a digital balance, a predetermined section of the patch needs to be divided into several pieces. The weights individually must be divided to determine the average weight and standard deviation values.

- According to Baichwal MR et al. Drug delivery system advancements, polymer films as drug delivery vehicles. The rolling ball tack test This test gauges a polymer's talk- related softness. A 7/16-inch-diameter stainless steel ball is thrown onto an inclined track in this test, allowing it to travel down and come into contact with horizontal, upward-facing adhesive. The amount of tack, measured in inches, is determined by how far the ball moves along the adhesive.
- According to Vyas SP, Khar RK et al. Novel carrier system for targeted and controlled drug delivery. pp. 411–447 in the first edition, New Delhi, CBS Publishers and Distributors, 2002. The produced patches are subjected to a drug release assessment using the paddle-over disc method (USP equipment V). A glass plate needs to be covered with an adhesive after dry films of a defined thickness are weighed and cut into precise shapes. Once the equipment is equilibrated to 32±0.5°C, the glass plate is submerged in 500 mL of the phosphate buffer (pH 7.4) or dissolving medium. At 50 revolutions per minute, the paddle is then moved to a distance of 2.5 cm from the glass plate. At suitable intervals for up to 24 hours, 5-mL aliquots of samples can be removed and examined using an HPLC or UV spectrophotometer.There is a possibility to calculate the mean value if the experiment is conducted in triplicate.
- According to Shaila L, Pandey S, Udupa N, et al. The creation and assessment of membrane-controlled matrix systems to break a strip, it must be sliced uniformly and folded repeatedly at the same spot. Folding endurance is measured by how many times a film can be folded in the same direction without breaking.
- According to Vyas SP, Khar RK et al. An in vitro permeation study can be conducted using a diffusion cell and full-thickness abdominal skin of male Westar rats. The skin should be carefully removed, cleaned, and equilibrated before starting the experiment. The cell temperature should be maintained at 32 ± 0.5°C using a thermostatically controlled heater. The skin piece should be mounted between compartments, with the epidermis facing upward. Sample volumes should be removed and replaced at regular intervals. Samples should be filtered and analysed spectrophotometrically or HPLC. Flux can be determined by dividing the flux by the initial drug load.
- According to Baichwal MR et al. With a speed of 12 inches per minute, the tape is removed from the substrate at a temperature of 90ºC. Tack value is measured and recorded as the peel force needed to break the binding between the adhesive and substrate. It is given in ounces or grammes per inch width.
- According to Baichwal MR et al. When a bond forms between the adhesive and the clean, precisely roughened probe tip, the adhesive is brought into contact with the tip. It is mechanically broken by taking the probe out later. Tack is a unit of measurement that represents the force needed to remove the probe from the adhesive at a predetermined pace in grammes.
- According to Vyas SP, Khar RK et al. Drug release studies conducted in vitro The produced patches are subjected to a drug release assessment using the paddle-over disc method (USP equipment V). A glass plate needs to be covered with an adhesive after dry films of a defined thickness are weighed and cut into precise shapes. Once the equipment is equilibrated to 32±0.5°C, the glass plate is submerged in 500 mL of the phosphate buffer (pH 7.4) or dissolving medium. At 50 revolutions per minute, the paddle is then moved to a distance of 2.5 cm from the glass plate. At suitable intervals for up to 24 hours, 5-mL aliquots of samples can be removed and examined using an HPLC or UV spectrophotometer. It is possible to calculate the mean value of the experiment if it is carried out in triplicate.
- According to Shivalingam et al. (2021) synthetic pantoprazole transdermal patches. One method of manufacturing that was used was solvent casting. The prospective film-forming polymers Eudragit L100, PVP K30, and HPMC E5 were investigated. Testing was done on the prepared patches for swelling index, % absorbed moisture, thickness, content homogeneity, folding durability, and in vitro drug release profile. It was determined that the best outcomes were obtained with patches

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containing the mixture Eudragit L100: HPMC E5 (1:1)

- According to Suhaitamy et al. (2021), They used several polymer combinations, such as PVP and HPMC, to make Meloxicam transdermal patches. Different amounts of propylene glycol, ranging from 10–30% w/v, were utilised as permeation enhancers. To create the patches, the solvent evaporation method was employed. The study's conclusions demonstrated that the improved patches possessed qualities that were appropriate for their kind.
- According to Sahu et al. (2021), Created hydrophobic and hydrophilic polymer ratio-based transdermal patches containing Dexamethasone and Ondansetron. The plasticiser used in the solvent casting process had a concentration of 15% w/v, whereas the penetration enhancer had a concentration of 5% w/v. Drug content, thickness, folding durability, tensile strength, and in vitro dissolution were among the distinctive qualities assessed for the optimised patches that were manufactured. Outcomes demonstrated that, in comparison to other polymers, EC patches had the superior qualities.
- According to Yasemin and Eme et al. (2021), Ready-made donepezil transdermal patches for Alzheimer's disease therapy. gelatine, sodium alginate, hydroxyethyl cellulose, and PVP were among the combinations of polymers that were investigated for use in patch manufacturing. Patches were made with Transcutol plasticiser. We used FT-IR for characterisation. Studies using Franz diffusion cells were used to release the drug from the prepared patches. Sustained drug release was demonstrated with PVP patches containing sodium alginate, according to the results.
- According to Malvey et al. (2021), Transdermal Ketorolac Tromethamine Patches manufactured. As film-forming polymers, HPMC E5 was employed. To play the part of plasticiser, PEG 400 was used. The formulation used DMSO as a permeation enhancer. The patches were prepared by the solvent casting process. Drug content, thickness, folding durability, tensile strength, and in vitro dissolution were among the distinctive qualities assessed for the optimised patches that were manufactured. The best formulations were determined to be patches containing HPMC E15 and medications in 200 mg doses with 8% DMSO.
- According to Patel et al. (2021), Ready-made transdermal Apixaban patches. In the matrix, rate-controlling polymers such as Eudragit RS100 and HPMC E50 LV were used. Purity enhancers and plasticisers, glycerine and PEG 400, were used, in that order. Any drug-polymer interactions were determined by FTIR analysis. % elongation, folding endurance, and appearance and weight variance were assessed for prepared batches of patches. The pH range of 6.8 to 7.1 was also observed in optimised patches containing a blend of polymers.

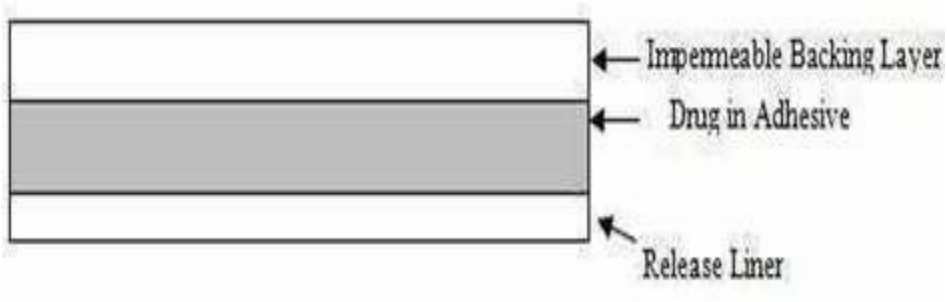

Fig. 1: Design Of Drug Inadhesive Type Transdermala Patch

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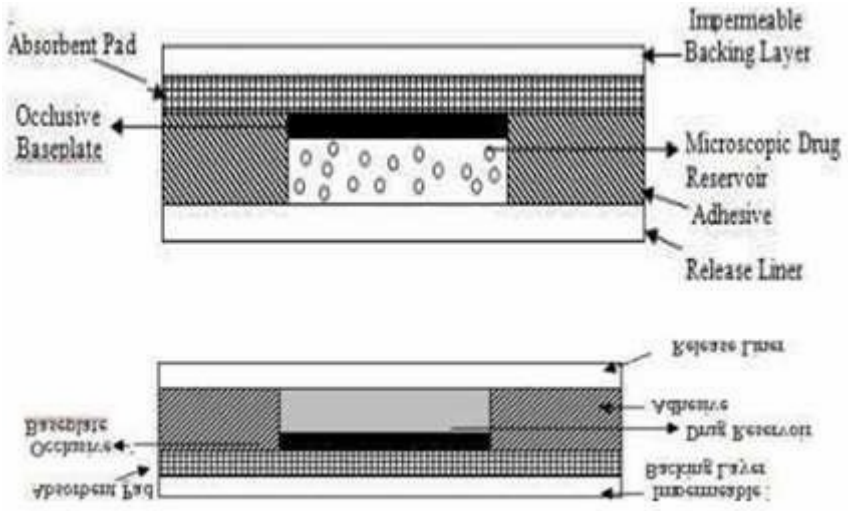

Fig. 2: Design of matrix-type transdermal patch

Advantages

- The technique is easy to use and just needs to be applied once a week. Patients who are intolerant to oral dosage forms may be able to get their medications via transdermal delivery, which offers an alternate mode of administration.
- Patients who are unconscious or experiencing nausea can benefit greatly from it.
- Since transdermal administration circumvents direct effects on the stomach and intestine, medications that disrupt the digestive system may be suitable candidates.
- Drugs that the gastrointestinal system's acids and enzymes break down could also be worthwhile targets
- Transdermal administration presents an additional advantage over oral drug delivery in that it circumvents first-pass metabolism.

Disadvantages

- The potential for localised discomfort when the product is applied.
- The medicine, the adhesive, or other excipients in the patch formulation may induce erythema, irritation, and local oedema.
- Possibly result in allergic responses.
- In order to be considered, the molecular weight must be less than 500 Da.
- Enough lipid and aqueous solubility; for permeate to cross SC and underlying aqueous layers, a log P (octanol/water) between 1 and 3 is necessary.

Drug/prodrug-

Drugs with unfavourable partition coefficients can now be delivered more effectively via the skin and transdermally thanks to the prodrug strategy. A moiety is included as part of the prodrug design in order to improve the parent drug's solubility and transport in the stratum corneum, as well as to raise the partition coefficient. Esters enhance a drug's solubility in the aqueous epidermis by hydrolysing it once it reaches the viable epidermis. Using 56-acyloxy methyl and 9-dialkyl amino methyl promoieties, for instance, the intrinsic low permeability of the highly polar 6-mercaptopurine was raised up to 240 times. More research has been done on the prodrug approach's capacity to increase the skin permeability of various medications, including alpha-blockers, naltrexone, buprenorphineand nalbuphine.

Liposomes and vehicles

Having the ability to encapsulate medications, liposomes are colloidal particles that develop as concentric bimolecular layers. Vesicles containing active chemicals are a common feature of cosmetic products. Enzymes, unscreening and tanning agents, humectants like urea and glycerol, etc. are some examples. While many other possible ingredients have been examined, phosphatidylcholine from soybean or egg yolk is the most commonly used composition. When cholesterol is added, it tends to stabilise the structure of the mixture and produces more stiff

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liposomes. How the stratum corneum absorbs medications more effectively is unknown. A portion of the stratum may be partially penetrated by the liposomes before they interact with the lipids in the skin to release their medicament, or only their constituent parts may reach it.

Solid lipid Nanoparticles-

As carriers for improved skin delivery of sunscreens, vitamins A and E, triptolide, and glucocorticoids, solid lipid nanoparticles (SLN) have recently been studied. An increase in skin hydration brought on by the occlusive layer that forms on the skin surfaces is regarded to be the main cause of their improved skin penetration

Iontophoresis-

By using a low-level electric current, either directly on the skin or indirectly through a dose form, this approach allows a topically applied medicinal material to permeate the skin. The kind of electrode, system pH, and current intensity are factors that influence the design of an ionophoretic skin delivery system. The mechanisms of electro-repulsion (for charged solutes), electro-osmosis (for uncharged solutes), and electro-perturbation (for both charged and uncharged) can be individually or in combination responsible for the increased drug penetration observed as a consequence of this technology.

Electroporation- It entails applying high-voltage pulses to the skin, which may cause temporary pores to appear. Treatment times of milliseconds and high voltages (100 V) are most commonly used. Small molecules, proteins, peptides, and oligonucleotides, as well as biopharmaceuticals with molecular weights more than 7kDA, have all been successfully enhanced in skin permeability by the application of this method

Ultrasound (sonophoresis and phonophoresis) In order to improve transdermal distribution of solutes, either concurrently or through pre-treatment, this technique uses ultrasonic energy. Skin permeability 7 is improved by applying low-frequency ultrasonography (55 kHz) for an average of 15 seconds.

Laser radiation and photomechanical waves-

Dermatological disorders like acne are commonly treated using lasers, which are also utilised to rejuvenate the face. In order to ablate the stratum corneum without seriously harming the underlying epidermis, this technique entails the direct and controlled application of a laser to the skin.

Radiofrequency-

In order to create heat-induced microchannels in the membrane, high-frequency alternating current must be applied to the skin. Both the quantity and depth of microchannels the gadget forms regulate the rate of drug delivery. Less than a second is spent on the treatment.

Magnetophoresis

The application of an external driving force in the form of a magnetic field to promote the diffusion of a diamagnetic solute through the skin. Alterations in the structure of the skin caused by exposure to a magnetic field may potentially enhance permeability.

Microneedle based devices- This approach served as the foundation for the first-ever drug delivery patents for topical medication administration. To get the medication to the SC and epidermis, these 50–110 micrometre long microneedles will pierce both.

Skin Abrasion-

By direct removal or disturbance of the skin's outer layers, the abrasion technique is employed. The superficial skin resurfacing methods doctors utilise to treat acne, scars, hyperpigmentation, and other skin imperfections constitute the basis for these devices.

EVALUATION PARAMETERS

Thickness of the patch

To confirm that the produced patch is the appropriate thickness, the thickness of the drug-loaded patch is measured using a digital micrometre at various spots. The average thickness and standard deviation are then calculated. A travelling microscope dial gauge, screw gauge, or micrometre is used at several film sites to measure the transdermal film's thickness.

Weight uniformity

Tests are conducted after the prepared patches have dried for four hours at 60°C. To weigh in a digital balance, a predetermined section of the patch needs to be divided into several pieces. The weights individually must be divided to determine the average weight and standard deviation values.

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Folding endurance

To break a strip, it must be sliced uniformly and folded repeatedly at the same spot. Folding endurance is measured by how many times a film can be folded in the same direction without breaking.

Moisture Uptake

A 24-hour period is spent storing weighed films at room temperature in desiccators. Then, using a saturated potassium chloride solution in desiccators, these are removed and exposed to 84% relative humidity until a consistent weight is reached. This is how the percentage of moisture uptake is computed.

Drug content

The task is to dissolve a given patch area in a given volume of an appropriate solvent. Next, the medicine must be added to the solution and filtered using a filter media (UV or HPLC procedure). Three distinct samples' averages are represented by each value.

Shear Adhesion test

An adhesive polymer's cohesive strength is to be determined by doing this particular test. There are several factors that can affect it, including the molecular weight, type, amount, and degree of cross-linking in the polymer. On a stainless-steel plate, an adhesive-coated tape is attached. To cause the tape to pull in a direction parallel to the plate, a precise weight is suspended from it. Timing the tape's removal from the plate allows one to calculate the shear adhesion strength. There is a direct correlation between shear strength and removal time.

Peel Adhesion test

Peel adhesion is the term used in this test to describe the force needed to remove an adhesive layer from a substrate. The variables that control peel adhesion capabilities are the type and quantity of additives, as well as the molecular weight of the adhesive polymer. The application of a single tape to a chosen backing membrane or stainless-steel plate is followed by a 180º angle pull of the tape from the substrate, at which point the force needed to remove the tape is measured.

Skin Irritation study

On healthy rabbits (average weight 1.2 to 1.5 kg), skin irritation and sensitisation testing can be carried out. The washing of the rabbit's dorsal surface (50 cm^2), shaving of the hair from that clean surface, and application of representative formulations can all be done there. The surface is cleansed with rectified spirit. In order to classify the skin injury into five grades based on severity, the patch must be removed after 24 hours and the skin examined.

Stability studies

The TDDS samples must be stored for six months at 40±0.5°C and 75±5% RH in order to undertake stability studies in accordance with ICH recommendations. In order to properly analyse the samples for drug content, they are removed at 0, 30, 60, 90, and 180 days.

II. CONCLUSION

Developed in 1981, transdermal drug delivery systems are a safe and efficient method of delivering drugs. Within the field of transdermal patches, significant advancements have been accomplished. Researcher interest in the Transdermal Drug Delivery System is high due to its many benefits. To integrate newer medications through this system, numerous new studies are being conducted now. Physicians may be able to give their patients more therapeutic options using transdermal dose forms, improving the quality of their care. Our knowledge of the characteristics of the stratum corneum barrier and the ways in which chemicals interact and affect its structure has improved recently because to the application of a number of biophysical approaches. The design of enhancers with ideal properties and low toxicity will be aided by a deeper comprehension of how enhancers interact with the stratum corneum and the establishment of structure-activity connections for enhancers. Regarding transdermal drug delivery systems and their review procedure in detail, this article offers helpful information.

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