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A REVIEW OF TRANSDERMAL PATCHES ON SKIN DISEASE

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Abstract

To address the challenges associated with drug delivery, particularly oral routes, transdermal drug delivery systems were introduced. An adhesive patch that has been medicated and applied to the skin to deliver a specified dosage of medication through the skin and into the bloodstream is called a transdermal patch. It encourages the body's wounded areas to mend. Transdermal drug delivery systems have an advantage over other forms of administration, such as oral, topical, intravenous, i.m., etc., in that the patient can administer medication in a controlled manner through the patch. Typically, this is achieved by either a porous membrane covering a reservoir of medication or by body heat melting thin layers of medication embedded in the adhesive. The fundamental drawback of transdermal administration methods is that because the skin acts as a very effective barrier, this form of delivery can only be used for drugs whose molecules are tiny enough to easily permeate the skin. The general introduction to transdermal patches, including their types, preparation techniques, and influencing factors, is covered in this review article.

Keywords: Transdermal drug delivery system; Hydrin rubber; Silicon rubber; Polyvinylalcohol; Transdermal patch; Polyvinylchloride; Di-N-butylphthalate;Triethylcitrate

Introduction

The oral route is the most widely used drug administration method; yet, it has several drawbacks, such as drug breakdown in the gastrointestinal tract due to pH and enzymes, first pass metabolism, etc. A unique medication delivery mechanism was created by Chien (1992), Banker (1990), and Guy (1996) in order to get around these issues. Transdermal delivery systems, or transdermal patches, were used. Medicated adhesive patches are created in this technology, and when applied to the skin, they distribute a therapeutically effective dosage of medication. They come in various sizes and contain multiple ingredients. After application to intact skin, they cross skin barriers to transfer the active components into the bloodstream. A transdermal patch that stays on the skin and contains a high dosage of medicationskin for an extended length of time, which diffuses into the bloodstream.

Three routes exist for drugs to enter the skin:

a) Through hair follicles.

b) By means of sebaceous glands.

c) Via the sweat duct.

Transdermal medication delivery devices are used to treat a variety of skin conditions, as well as neurological conditions like Parkinson's disease, angina pectoris, aches, and quitting smoking

Literature Review

1. **Niha Sultana *et al. 2023*:** "issolving microneedle transdermal patch loaded with Risedronate sodium and Ursolic acid bipartite nanotransfersomes to combat osteoporosis: Optimization, characterization.

2. **Deepak Thakur *et al. 2023*:** Removal of mandibular third molars surgically is one of the most frequently performed oral surgical procedures which are often accompanied with post-operative pain, swelling and trismus

3. **Shivaprasad Gadag *et al. 2023*:** Resveratrol (RVT) is a polyphenolic phytoestrogen which has shown antiproliferative activity in breast cancer."

4. **Veerabahu Subbukutti *et al. 2023*:** The wound-healing process is accelerated by inhibiting proteins that decelerate the wound-healing pathway. "

5. **Suhela Tyeb *et al. 2023*** Polysaccharides form a major class of natural polymers with diverse applications in biomedical science and tissue.

6. **Rajwant Kaur *et al. 2023***Transdermal patches are the cutting-edge drug delivery approach that may be utilized to bypass hepatic first-pass metabolism and to increase absorption for effective systemic effects"

7. **Reetu Chauhan *et al. 2023*:** A self-contained, covert, medicated adhesive patch known as a transdermal patch offers a practical mode of delivery for a range of skin and body problems.

8. **Deepankar Shukla *et al. 2023*:** Diclofenac sodium is a nonsteroidal anti- inflammatory drug that

effectively manages pain following therapeutic extractions.

9. **Bungorn Sripanidkulchai *et al. 2023*:** Kaempferia parviflora and Curcuma longa have been widely reported to have a potent anti-inflammatory effect.

10. **Monika Bhairam *et al. 2023***: here is a global epidemic of chronic diseases like diabetes mellitus and systemic hypertension. Diabetes mellitus is typically accompanied by systemic hypertension, and often vice versa.

11. **Pooja Dhama *et al. 2023*:** Transdermal drug delivery leads direct access to the systemic circulation through the skin which bypass drug from the hepatic first pass metabolism leading to increase bioavailability

12. **Dildar Khan *et al. 2023*:** To formulate and evaluate a pH-responsive nanoparticle (NP)-based patch for efficient transdermal delivery of flurbiprofen against rheumatoidarthritis

13. **Dildar Khan *et al. 2023*:** The administration of pioglitazone as an oral therapy is restricted due to various challenges. The aim of the current investigation was to evaluate the suitability of pioglitazone in adhesive transdermal patch as an alternativedelivery system, in order to improve therapeutic delivery. "2019

14. **Mahesh Attimarad *et al. 2023*:** Transdermal patches were formulated using permeation enhancer namely T-Anethole. Zidovudine patches were prepared by solvent casting method.

15. **Hameed *et al. 2023*:** Transdermal patches can be tailored and developed according to the physicochemical properties of active and inactive components, and applicability for long-term use, and a number of chemical approaches and physical techniques for transdermal patch development are under"

Types of Transdermal Drug Delivery System

Single-layer Drug-in-Adhesive System:

The medication is contained in the system's sticky layer in this kind of patch. Not only does the adhesive layer help to bind the several layers together and the system to the skin, but it also releases the medication. A backing and a temporary liner encircle the adhesive layer.

Reservoir System:

The drug reservoir in this system is maintained between a rate-controlling membrane and a backing layer. the medication releases via a rate-controlled microporous membrane. The drug may be distributed throughout the reservoir compartment as a solid polymer matrix or as a gel, suspension, or solution.

Matrix System: This system is of Two type

Drug-in-Adhesive System: To create a drug reservoir, the drug is first dissolved in an adhesive polymer, and the medicated polymer adhesive is then applied by solvent casting or, in the case of hot-melt adhesives, by melting the adhesive onto an impermeable backing layer.

b) Matrix-Dispersion System: In this system, a hydrophilic or lipophilic polymer matrix evenly distributes the medication. Additionally, this drug-containing polymer is attached onto an occlusive base plate within a compartment made of a backing layer that is impermeable to drugs. Instead of placing the adhesive on the drug reservoir's face to create an adhesive rim strip, this approach spreads it around the circle

Micro-Reservoir System:

This system combines matrix-dispersion and reservoir technologies. This involves suspending the medication in an aqueous solution of a water-soluble polymer and evenly spreading the solution in a lipophilic polymer to create thousands of microscopic, unleachable drug reservoir spheres

Components of Transdermal Drug Delivery System

- Polymer matrix/Drug reservoir
- Drug
- Permeation enhancers.
- Pressure sensitive adhesive (PSA).
- Backing laminate.
- Release liner.
- Other excipients like plasticizers and solvents

Polymer Matrix/ Drug Reservoir:

The medication is manufactured by dispersing it in a synthetic polymer basis, either in liquid or solid state. It should be chemically and biocompatible with the medicine as well as other system components like penetration enhancers. They should also be safe and distribute a drug consistently and effectively for the duration of the product's stated shelf life. The following categories apply to polymers used in transdermal medication delivery systems:

Natural Polymers: e.g. cellulose derivatives, zein,gelatin, shellac, waxes, gums, naturalrubber and chitosanetc.

Synthetic Elastomers: e.g. polybutadiene, hydrinrubber, silicon rubber, polyisobutylene, acrylonitrile,neoprene, butyl rubber etc.

Synthetic Polymers: e.g. polyvinylalcohol,polyvinylchloride, polyethylene,polypropylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone,polymethylmethacrylate etc [6,7].

Drugs: The following are some excellent medication qualities and things to keep in mindwhen making transdermal patches:

Ideal Properties of Drugs: (Table1)

S.No.	Parameter	Properties
1	Dose	Should be Low in weight (less than20mg/day).
2	Half-life	10/less(hrs).
3	Molecularweight	<400da.
4	Skinpermeability coefficient	>0.5*10-3cm/h.

5	SkinReaction	Nonirritating,Nonsensitizing
6	Oralbioavailabilit	Low.

Permeation Enhancers:

the substances that improve stratum corneum permeability in order to achieve therapeutic concentrations of the medication candidate. They interact with the stratum corneum to increase permeability.

a) The Perfect Features of Enhancers for Permeation

i. They must not cause irritation, be poisonous, or cause allergies.

ii. They must not have any pharmacological action, that is, they must not bind to the receptorsite.

iii. They ought to have a suitable skin sensation and be aesthetically pleasing. [8]

Pressure Sensitive Adhesive (PSA):

It facilitates a transdermal patch's increased adhesion to the skin's surface. It may be removedfrom the smooth surface with ease and without leaving any trace.

Adhesives based on silicon;.Polyisobutylene

Polyacrylates

Backing Laminate: It's a supporting substance that doesn't let medicines or penetration enhancers pass through. They ought to be chemically compatible with the excipients, adhesive, enhancer, and medication.

For example, vinyl, polyester, and polyethylene films

Release Liner:

The main packing material that can shield the patch while it's being applied is this one. Its base layer is composed of either an occlusive (like paper fabric) or non-occlusive (like polyethylene, polyvinyl chloride) material.

Teflon or silicon make up its composition. The release liner needs to be permeable to drugs,penetration enhancers, and water in addition to being chemically inert.

Other Excipients Like Plasticizers andSolvents

Solvents: Chloroform, methanol, acetone, isopropanoland dichloromethane.

Plasticizers: Dibutyl pthalate, triethylcitrate, polyethylene glycol and propylene glycol[10].

Methods of Preparation of TDDS
Asymmetric TPX membrane method.

Permeation Enhancers:

Circular Teflonmould method.Mercury

substrate method.

Byusing “IP Mmembranes” method. Byusing “EVAC

membranes” method.

PreparationofTDDSbyusingProliposomes.Byusing free film

method

Asymmetric TPX Membrane Method:

Berner and John made this technique known in 1994. Using heat sealable polyester film (type 1009, 3m) with a 1cm diameter concave as the backing membrane, a prototype patch can be made using this procedure. The drug was spread out on a concave membrane, sealed with an adhesive, and coated with an asymmetric TPX [poly (4-methyl-1-pentene)] membrane.

Preparation:

The dry or wet inversion procedure is used to prepare them. In order to create a polymer solution, TPX is dissolved in a mixture of solvent (cyclohexane) and non-solvent additives at 60°C. After 24 hours at 40°C, the polymer solution is cast onto a glass plate. After 30 seconds of evaporation at 50°C, the glass plate must be promptly submerged in a coagulation bath with a temperature maintained at 25°C. The membrane can be removed after 10 minutes of immersion and allowed to air dry for 12 hours at 50°C in a circulation oven.

Circular Teflon Mould Method:

Baker and Heller made the discovery in 1989. Different ratios of polymeric solution are utilised as organic solvents. After then, the solution is split into two sections. A certain quantity of the medication is dissolved in one portion, and variable concentrations of enhancers are dissolved in another, before the two parts are combined. Next, plasticizer is added to the drug polymer solution, such as Di-N-butylphthalate. After 12 hours of stirring, the entire mixture should be put 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. And thena dried film developed, which, in order to prevent the effects of ageing, must be kept for a further 24 hours at 25±0.5°C in a desiccator filled with silica gel.

Mercury Substrate Method:.

This process involves dissolving the medication and plasticizer in the polymeric solution. After agitating for ten to fifteen minutes to achieve a uniform dispersion, the mixture is

poured onto a levelled mercury surface and covered with an inverted funnel to regulate the evaporation of the solvent.

By Using “IPM Membranes” Method:

The medication is dissolved in the water and polymer mixture (propylene glycol with Carbomer 940 polymer) and is agitated with a magnetic stirrer for a duration of 12 hours. Triethanolamine is to be added to the dispersion in order to neutralise it and make it viscous. Buffer pH 7.4 is used to create solution gel in cases where the drug's solubility in aqueous solution is extremely low. The IPM membrane will incorporate the gel that has produced.

By Using “EVAC Membranes” Method:

Polyethelene (PE), ethylene vinyl acetate copolymer (EVAC) membrane, and 1% carbopol reservoir gel are required as rate control membranes for the manufacture of TDS. For the manufacture of gels, utilise propylene glycol if the medication is insoluble in water. Propylene glycol is used to dissolve the drug. Carbopol resin is then added to the mixture and neutralised using 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 edges will be heated toseal.

Preparation of TDDS by Using Proliposomes:

Proliposomes are made via the film deposition process with a carrier approach. The ideal drug to lecithin ratio, as determined by earlier sources, is 0.1:2.0. 5 mg of mannitol powder is used to manufacture proliosomes in a 100 ml round-bottom flask. The flask is then held at a temperature between 60 and 70 °C, spun at 80 to 90 rpm, and vacuum-dried for 30 minutes. The water bath's temperature is changed to between 20 and 30°C after drying. A 0.5 ml aliquot of the organic solution is added to the round-bottomed flask at 37°C after the drug and lecithin have been dissolved in an appropriate organic solvent mixture. After the solution has completely dried, another 0.5 ml aliquot of the solution is to be added. Following the last loading, the proliposome-containing flask islinked in a lyophilizer, after which drug-loaded mannitol powders (proliposomes) are left overnight in adesiccator before being sieved through a 100 mesh screen. Until it is characterised, the gathered powder is kept at the freezing temperature in a glass bottle.

By using Free Film Method:

Using this method, cellulose acetate-free film is initially made by casting it onto a mercury surface. Chloroform is also used to prepare a 2% w/w polymer solution. At a concentration of 40% w/w of polymer weight, plasticizers have to be applied. Next, a glass ring with 5 ml of the polymer solution is poured into it and set over the mercury surface in a glass petridish. By covering the petridish with an inverted funnel, the solvent's rate of evaporation can be regulated. Upon full solvent evaporation, the mercury surface is observed to detect the

creation of a layer. After being separated, the dry film will be kept in a desiccator in betweenthe wax paper sheets until it is needed. We may create free films using this method.

Factors Affecting Transdermal Patches

There are various factors which affects the action of transdermal patches. These are givenbelow:

1.Physicochemical Properties2.Partition co

efficient 3.Mole cularsize

4.Solubility/melting point 5.Ionization

6.Physiological & Pathological Conditions of Skin7.Reservoir effect of horny

layer

8.Lipid film 9.Skin hydration

10.Skin temperature 11.Regional variation

12. Pathological injuries to the skin

13. Cutaneous self-metabolism

14.Skin barrier properties in the neonate and young infant15.Skin barrier

properties in aged skin

16. Race

17. Bodysite

18. Penetration enhancers used

Benefits

a) Drug metabolisms that are first pass are avoided.

b) Incompatibilities with the digestive system are avoided.Self-medication

is a viable option.

d) The action becomes more prolonged and predictable.

e) Unwanted effects are reduced.

f) The drug plasma concentration is kept constant.

g) Less doses are administered, which enhances patient compliance.

h) Avoiding drug-related issues such as decreased absorption, GI discomfort, and breakdown resulting from hepatic first pass metabolism increases the therapeutic efficacy of several medications [14, 15].

Disadvantages

a. Potential allergic reactions, such as itching, rashes, local edoema, etc., at the application site.

b. Drugs with larger molecular sizes (over 1000) have more difficulty being absorbed.

c. The skin's barrier function varies depending on the individual and the location.

d. Due to their lower permeability, drugs with hydrophilic character are less suited than those with lipophilic character [16].

Future of Transdermal Drug Delivery System

Future developments in drug delivery systems will involve microemulsion, liposomes, and niosomes. The purpose of this discovery is to enhance medication delivery, as the majority of classical formulation excipients have limited intrinsic solubility. Numerous medications, including steroids, methotrexate, interferon, antifungals, and antibiotics, are being developed for possible administration. Transdermal patch sales are expected to rise in the future and have grown at a rate of 25% annually in previous years. As new devices are developed and the number of transdermal drugs that are marketed rises, this number will rise in the future. As long as design advancements are made, transdermal analgesic administration is expected to gain more and more traction. Studies are being conducted to improve efficacy andsafety. To enhance practical issues such the patch wearer's experience, as well as to distribute medication more precisely and for a longer period of time. Improved transdermal technology, which uses mechanical energy to boost drug flux through the skin by changing the skin barrier or raising the energy of the drug molecules, is another possible enhancement. Following the successful development of iontophoresis patches, further "active" transdermal technologies are being researched for a range of medications. These include sonophoresis, which uses low frequency ultrasonic energy to disrupt the stratum corneum, thermal energy, which uses heat to increase the energy of drug molecules and make the skin more permeable, and electroporation, which uses short electrical pulses of high voltage to create transient aqueous pores in the skin. Magnetophoresis, or magnetic energy, has been looked into as a way to boost medication flow through the skin. It's possible that the transdermal patch is a neglected method for treating both acute and chronic pain. We anticipate that this drug delivery mode will become more widely used and applicable due to its enhanced delivery and expanded selection of analgesics. With almost 40% of drug delivery candidate items undergoing clinical trials connected to transdermal or dermal systems, transdermal drug delivery systems are now the most successful novel research area in new drug delivery systems when compared to oral treatments. The safest, easiest, and substitute method for systemic medication delivery is the transdermal drug delivery system (TDDS). Systemic

medication delivery through the epidermis has a number of benefits, including upkeep Steady medication levels in the plasma, less adverse effects, enhanced bioavailability through hepatic first pass metabolism

bypass, and improved patient adherence to treatment regimens are essential. Skin is now thought to be the safest route for administering drugs since it allowsfor continuous drug release into the bloodstream [17].

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