International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

A Brief Review on Transdermal Patches

Authors:-Ranjit Subhash jadhav, Prof. Neha B. Gaikwad, Dr. Kawade R.M.
Nandkumar Shinde College Of Pharmacy , Vaijapur- 423701

Date of Submission: 20-11-2024 Date of Acceptance: 30-11-2024

ABSTRACT:
Transdermal drug delivery system was presented to overcome the difficulties of drug delivery especially oral route. A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. It promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of delivery system such as oral, topical, i.v, i.m, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The main disadvantage to transdermal delivery systems stems from the fact that the skin is a very effective barrier, as a result, only medications whose molecules are small can easily penetrate the skin, so it can be delivered by this method. This review article describes the overall introduction of transdermal patches including type of transdermal patches, method of preparation of transdermal patches and factor affecting etc.

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

I. INTRODUCTION:

The oral route is the most commonly used method for delivering drugs. However, it does have drawbacks such as first-pass metabolism. Degradation of drugs in the gastrointestinal tract is caused by enzymes and pH levels. In order to address these issues, a new method of delivering drugs was developed. Chien created it in 1992, while Banker developed it in 1990 and Guy in 1996. This one Transdermal patches or Transdermal delivery system were used. Text, the same input language and the same amount of words will be used to paraphrase the original text.Medicated adhesive patches within a system are formulated to administer a sufficient quantity of medication is delivered through the skin for therapeutic benefit It was positioned on the skin. They come in various sizes and are equipped with. Multiple ingredients. When they are put on intact skin They distribute active substances through the bloodstream, entering systemic circulation. Through cutaneous barriers. A patch with a concentrated dosage is designed to be applied on the skin. Medication contained within that remains on the skin for an extended period of time. Time enters the bloodstream through a process of diffusion.

There are three ways in which drugs can enter the skin.

a) Via hair follicles.
b) Via sebaceous glands.
c) Via the sweat duct.

Transdermal drug delivery systems are employed for different skin applications. Issues, as well as in the treatment of chest pain, aches quitting smoking can reduce the risk of developing neurological conditions like Parkinson‟s disease Illness[1,2].

Types of Transdermal Drug Delivery System:
Single-layer Drug-in-Adhesive System:

In this kind of patch the drug is contained within the adhesive layer of this system. The glue Layer functions not just to stick the different layers together, but Controlling not only the outer layer of the skin, but also for regulating the entire system. The drug being released. The adhesive layer is encased by a temporary lining and a support.

Reservoir System:

The drug reservoir is stored in this system. Between the backing layer and a membrane that controls the rate. Drug is released at a controlled rate through microporous materials. Membrane. Medication may exist as a solution, suspension, or gel, or it can be spread out within a solid polymer matrix located in the reservoir. A section or division of a larger space.(Figure 1)

Matrix System:

This system comes in two varieties.
A) Drug-in-Adhesive System: To create drug delivery system the drug is distributed within an

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

adhesive polymer reservoir. Spreading the adhesive polymer treated with medication using solvent creating or liquefying the bond (for hot-melt applications) Applying an adhesive onto a waterproof backing layer.

B) Matrix-Dispersion System: Drug is dispersed in a matrix within this system. Is evenly distributed in a hydrophilic or lipophilic manner. Synthetic material. And this polymer that contains a medication is attached to a sealed base plate within a section. Made from a backing layer that does not allow drugs to pass through. In this particular situation the adhesive is evenly distributed around the edge of the system. Applying on the face of the drug reservoir to create a adhesive border strip.[3].

Micro-Reservoir System:

This system is a combination of water reservoirs and matrix dispersion systems. Where the drug Is suspended in an aqueous solution of a water-soluble polymer, the solution is then uniformly dispersed in the lipophilic polymer to form thousands of dense microspheres Of drug reservoirs[4].

Components of Transdermal Drug Delivery System:

a) Polymer matrix/ Drug reservoir
b) Drug
c) Permeation enhancers.
d) Pressure sensitive adhesive (PSA).
e) Backing laminate.
f) Release liner.
g) Other excipients like plasticizers and solvents [5].

Polymer Matrix/ Drug Reservoir:

The formulation involves the dispersion of the drug within a synthetic polymer matrix, which can be in either liquid or solid form. It is essential that this matrix exhibits both biocompatibility and chemical compatibility with the drug and other system components, such as penetration enhancers. Furthermore, the system must ensure reliable and effective drug delivery throughout its designated shelf life while maintaining safety standards. The polymers utilized in transdermal drug delivery systems can be categorized into the following groups:

A) Natural Polymers: including cellulose derivatives, zein, gelatin, shellac, waxes, gums, natural rubber, and chitosan.

b) Synthetic Elastomers: such as polybutadiene, hydrin rubber, silicone rubber, polyisobutylene, acrylonitrile, neoprene, and butyl rubber.

c) Synthetic Polymers: comprising polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene, polyacrylate, polyamide, polyurea, polyvinylpyrrolidone, and polymethyl methacrylate [6,7].

Drugs:

Certain optimal characteristics of drugs and various factors that should be taken into account during the formulation of transdermal patches are outlined as follows.

a. Ideal Properties of Drugs: (Table 1)

Sr. No	Parameter	Properties
1.	Dose	Should be Low in weight(lessthan 20mg/day).
2.	Half-life	10/less (hrs).
3.	Molecular weight	<400da.
4.	Skin permeability coefficient	>0.5*10-3cm/h.
5.	Skin reaction	Non irritating, Non sensitizing
6.	Oral bioavailability	Low.

b. Factors Affecting: (Table 2)

Physicochemical	Pharmacokinetic	Biological
Stability	Half-life	Skin toxicity
Crystallinity	Volume of distribution	Site of application
Molecular weight	Total body clearance	Allergic reaction
Polarity	Therapeutic plasma conc	Skin metabolism
Melting point	Bioavailable factor	

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

Permeation Enhancers:
These are chemical agents that facilitate the increased permeability of the stratum corneum, thereby enabling the achievement of therapeutic concentrations of the drug candidate. Their mechanism of action involves interaction with the stratum corneum to enhance drug absorption.
a) Desired Characteristics of Permeation Enhancers
i. They must be non-irritating, non-toxic, and non-allergenic.
ii. They should not interact with receptor sites, meaning they should not exhibit any pharmacological effects.
iii. They ought to be cosmetically acceptable, providing a suitable sensory experience on the skin [8].

Pressure Sensitive Adhesive (PSA):
Pressure Sensitive Adhesive (PSA) plays a crucial role in enhancing the adhesion of transdermal patches to the skin. It is designed for easy removal from smooth surfaces, ensuring that no residue remains post-application. The types of PSAs include:
a) Polyacrylates
b) Polyisobutylene
c) Silicone-based adhesives.

Backing Laminate: This is a supportive material that is resistant to both drugs and permeation enhancers. It must exhibit chemical compatibility with the drug, enhancer, adhesive, and other excipients. Examples include films made from vinyl, polyethylene, and polyester [9].
Release Liner: This component serves as the main packaging material that safeguards the patch during its application. It consists of a base layer that can be classified as either
a) Non-occlusive (such as paper fabric) or

b) Occlusive (for instance, polyethylene or polyvinyl chloride).

The liner is typically composed of silicone or Teflon. It is essential for the release liner to be chemically inert while also allowing permeability to the drug, penetration enhancers, and water.

Other Excipients Like Plasticizers and Solvents:
a) Solvents include chloroform, methanol, acetone, isopropanol, and dichloromethane.
b) Plasticizers consist of dibutyl phthalate, triethyl citrate, polyethylene glycol, and propylene glycol [10] .

Methods of Preparation of TDDS:
a) Asymmetric TPX membrane method.
b) Circular Teflon mould method.
c) Mercury substrate method.
d) By using “IPM membranes” method.
e) By using “EVAC membranes” method.
f) Preparation of TDDS by using Proliposomes.
g) By using free film method.

Asymmetric TPX Membrane Method:

This technique was introduced by Berner and John in 1994. It involves the preparation of a prototype patch utilizing a heat sealable polyester film (type 1009, 3M) as the backing membrane, featuring a concave shape with a diameter of 1 cm. The drug is applied to the concave surface, which is subsequently covered with an asymmetric TPX [poly (4-methyl-1-pentene)] membrane and sealed using an adhesive.

Preparation: The membranes can be fabricated through either a dry or wet inversion process. In this approach, TPX is dissolved in a solvent mixture (cyclohexane) combined with non-solvent additives at a temperature of 60°C to create a polymer solution. This solution is maintained at 40°C for 24 hours before being cast onto a glass plate. The casting film undergoes evaporation at 50°C for 30 seconds, after which the glass plate is immersed in a coagulation bath maintained at 25°C. Following a 10-minute immersion period, the membrane is removed and air-dried in a circulating oven at 50°C for 12 hours.

Circular Teflon Mould Method:

Discovered by Baker and Heller in 1989, this method employs a polymeric solution in varying proportions as an organic solvent. The solution is divided into two components: one containing a calculated amount of drug and the other containing enhancers at different concentrations. These two components are then combined. A plasticizer, such as Di-N-butylphthalate, is incorporated into the drug-polymer solution. The entire mixture is stirred for 12 hours before being poured into a circular Teflon mould. The moulds are placed on a leveled surface and covered with an inverted funnel to regulate solvent vaporization within a laminar flow hood operating at an air speed of 0.5 m/s. The solvent is allowed to evaporate for 24 hours, resulting in a dried film, which is then stored for an additional 24 hours at 25±0.5°C in a desiccator containing silica gel to mitigate aging effects.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

Mercury Substrate Technique:

This technique involves dissolving the drug and plasticizer within a polymeric solution. The mixture is stirred for a duration of 10 to 15 minutes to achieve a uniform dispersion, which is subsequently poured onto a leveled mercury surface. An inverted funnel is then placed over the setup to regulate the evaporation of the solvent.

IPM Membranes Technique:

In this approach, a combination of water and polymer (specifically, propylene glycol containing Carbomer 940) is utilized to disperse the drug, which is stirred for 12 hours using a magnetic stirrer. The resulting dispersion is neutralized and thickened through the addition of triethanolamine. In cases where the drug exhibits poor solubility in aqueous solutions, a gel is formed by employing a buffer with a pH of 7.4. This gel is then incorporated into the IPM membrane.

EVAC Membranes Technique:

For the formulation of transdermal delivery systems (TDS), a 1% carbopol reservoir gel, along with polyethylene (PE) and ethylene vinyl acetate copolymer (EVAC) membranes, is required to serve as the rate-controlling membrane. In instances where the drug is insoluble in water, propylene glycol is utilized for gel preparation. The drug is dissolved in propylene glycol, to which carbopol resin is added and subsequently neutralized with a 5% w/w sodium hydroxide solution. The drug, now in gel form, is applied to a backing layer covering the designated area. A rate-controlling membrane is then placed over the gel, and the edges are sealed through heat application to create a leak-proof device.

Preparation of TDDS Utilizing Proliposomes:

Proliposomes are synthesized through the carrier method employing a film deposition technique. An optimal drug-to-lecithin ratio of 0.1:2.0, as established in prior studies, is utilized. In a 100 ml round-bottom flask, 5 mg of mannitol powder is introduced and maintained at a temperature of 60-70°C while the flask is rotated at 80-90 rpm. The mannitol is subjected to vacuum drying for a duration of 30 minutes. Following this drying phase, the water bath temperature is adjusted to 20-30°C. The drug and lecithin are dissolved in an appropriate organic solvent mixture, and a 0.5 ml aliquot of this organic solution is added to the round-bottom flask at 37°C. Upon complete evaporation, a second aliquot of 0.5 ml is introduced. After the final loading, the flask containing the proliposomes is connected to a lyophilizer. The drug-loaded mannitol powders (proliposomes) are then placed in a desiccator overnight and subsequently sieved through a 100 mesh screen. The resulting powder is transferred to a glass container and stored at freezing temperatures until further characterization.

When using the free film method:

In this process, a non-acetate cellulose layer is first deposited by casting on the mercury surface. And 2% w/w polymer solution is prepared using chloroform. Detergents should be added at a concentration of 40 percent by weight of the polymer. Then pour 5 ml of polymer solution into a glass ring and place it on the surface of mercury in a glass Petri dish. The rate of solvent evaporation can be controlled by placing a rotating funnel on a Petri dish. Film formation is determined by observing the mercury level After evaporation of the solvent. The dry film is separated and stored in a desiccator between sheets of wax for use. With this process, we can produce free films of different thicknesses, produced by changing the volume of the polymer solution[11,12]

Factors Affecting Transdermal Patches:

There are various factors which affects the action of Transdermal patches. These are given below:

a. Physicochemical Properties
i. Partition coefficient
ii. Molecular size
iii. Solubility/melting point
iv. Ionization
b. Physiological & Pathological Conditions of Skin
i. Reservoir effect of horny layer
ii. Lipid film
iii. Skin hydration
iv. Skin temperature
v. Regional variation
vi. Pathological injuries to the skin
vii. Cutaneous self-metabolism
viii. Skin barrier properties in the neonate and young infant
ix. Skin barrier properties in aged skin
x. Race
xi. Body site
xii. Penetration enhancers used [13].

Advantages of TDDS:

1. Transdermal administration guarantees a continuous and persistent penetration of a drug

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

over a prolonged duration, hence preventing first-pass metabolism [14].
2. Boost adherence from patients.
3. It does not affect the stomach or intestines‟ fluids [5].
4. Maintains steady and consistent blood levels, giving long-term control [16, 17].
5. Decreased medication plasma concentration levels.
6. Reduce medication variations in plasma levels and use drug candidates with low therapeutic indices and short half-lives [18].
7. It is simple to stop drug administration in cases of toxicity.
8. Lower the frequency of medication and improve patient adherence [19].
9. Many medications are more effective when administered transdermally because it avoids problems with the medication, like poor absorption and gastric discomfort.
10. Reduced variations in drug reaction within and between patients are the outcome of the simplified medication plan .

Disadvantages of TDDS:
1. For the medicine to pass through the stratum corneum, it needs to have advantageous physicochemical characteristics.
2. When it comes to daily dosages, the drug quantity should not be more than 5 mg; if it is, transdermal drug distribution becomes difficult.
3. The medication, adhesive, and additional chemicals in the patch may irritate the skin locally.
4. To use the transdermal delivery system, a specific clinical need needs to be established.
5. High drug concentrations in plasma or blood could not be attained [20].
6. Drugs with large molecular sizes cannot be synthesized.
7. Potential for irritation at the application site [21].
8. Wearing it is uncomfortable.
9. It might not be cost-effective.
10. Each person has a different skin barrier, and it can even alter over time within the same individual [22].

Future of Transdermal Drug Delivery System:

Future developments in drug delivery systems encompass liposomes, niosomes, and microemulsions. The primary objective of these advancements is to enhance the delivery of drugs that exhibit low solubility in conventional formulation excipients. A diverse array of potential drugs, including steroids, antifungals, antibacterials, interferon, methotrexate, and local anesthetics, is being formulated for effective delivery. The market for transdermal patches is projected to grow significantly, having recently experienced an annual growth rate of 25%. This trend is expected to continue as innovative devices are introduced and the range of marketed transdermal drugs expands. The transdermal delivery of analgesics is anticipated to gain further traction as design improvements are made. Ongoing research aims to enhance both safety and efficacy, focusing on optimizing the user experience of the patch and ensuring more accurate drug delivery with extended duration of action. Additional potential advancements include the development of transdermal technologies that employ mechanical energy to enhance drug flux across the skin, either by modifying the skin barrier or by increasing the energy of the drug molecules. Following the successful design of patches utilizing iontophoresis, various methodologies are being explored. Research is currently being conducted on various „active‟ transdermal technologies for the delivery of different medications. These technologies encompass electroporation, which employs brief high-voltage electrical pulses to create temporary aqueous pores in the skin; sonophoresis, which utilizes low-frequency ultrasonic energy to disrupt the stratum corneum; and thermal energy, which applies heat to enhance skin permeability and elevate the energy of drug molecules. Additionally, magnetophoresis, a method that uses magnetic energy, has been explored to facilitate increased drug flux through the skin. The transdermal patch represents a potentially underutilized resource for managing both acute and chronic pain. With advancements in drug delivery and a broader selection of analgesics, it is anticipated that the acceptance and use of this method will grow. Presently, the transdermal route of drug delivery is regarded as one of the most promising areas of innovative research, particularly when compared to oral treatments, with approximately 40% of drug delivery candidates undergoing clinical trials related to transdermal or dermal systems. Transdermal drug delivery systems (TDDS) have been developed as a safer and more convenient alternative for systemic drug administration. Administering drugs through the skin offers several benefits, including the maintenance of stable drug levels in the bloodstream, a reduction in side effects, enhanced bioavailability by bypassing hepatic first-pass metabolism, and improved patient adherence to

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 6 Nov - Dec 2024, pp: 526-532 www.ijprajournal.com ISSN: 2456-4494

treatment regimens. Recently, the skin has been recognized as a secure route for drug administration, allowing for continuous drug release into systemic circulation [23].

REFERENCES:

[1]. Arti Kesarwani, Ajit Kumar Yadav, Sunil Singh, Hemendra Gautam, Haribansh N Singh, et al. (2013) A review-Theoretical aspects of Transdermal Drug Delivery System. Bulletin of Pharmaceutical Research 3(2): 78-89.

[2]. Sampath Sampath Kumar KP, Debjit Bhowmik, Chiranjib B, RM Chandira (2010) A review- Transdermal Drug Delivery System- A Novel Drug Delivery System and its market scope and opportunities. International Journal of Pharma and Bio Sciences 1(2).

[3]. Saurabh Pandey, Ashutosh Badola, Ganesh Kumar Bhatt, Preeti Kothiyal (2013) An Overview on Transdermal Drug Delivery System. International Journal of Pharmaceutical and Chemical sciences 2(3).

[4]. P K Gaur, S Mishra, S Purohit, K Dave (2009) Transdermal Drug Delivery System: AReview. Asian Journal of Pharmaceutical and Clinical Research 2(1): 14-20.

[5]. Vandana Yadav, Sipia Altaf Bhai M, Mamatha Y, Prashant VV (2012) Transdermal Drug Delivery System: A Technical Writeup. Journal of Pharmaceutical & Scientific innovation 1(1).

[6]. Nikhil Sharma, Bharat Parashar, Shalini Sharma, Uday Mahajan (2012) Blooming Pharma Industry with Transdermal Drug Delivery System. Indo Global Journal of Pharmaceutical Sciences 2(3): 262-278.

[7]. Saurabh Pandey, Ashutosh Badola, Ganesh Kumar Bhatt, Preeti Kothiyal An Overview on Transdermal Drug Delivery System. International Journal of Pharmaceutical and Chemical sciences.

[8]. Kamal Gandhi, Anu Dahiya, Monika, Taruna Karla, Khushboo Singh Transdermal drug delivery-A Review.

[9]. K Ezhumalai, P Ilavarasan, R Murali Mugundhan, U Sathiyaraj, AN Rajalakshmi (2011) Transdermal Patches in Novel Drug Delivery System. International Journal of Pharmacy & Technology 3(2): 2402-2419.

[10]. Hiren J Patel, Darshan G Trivedi, Anand K Bhandari, Dushyant A Shah (2011) Penetration enhancers for Transdermal Drug Delivery System: A Review. IJPI‟s Journal of Pharmaceutics and Cosmetology 1(2).

[11]. J Ashok Kumar, Nikhila Pullakandam, S Lakshmana Prabu, V Gopal (2010) Transdermal Drug Delivery System: An Overview. International Journal of Pharmaceutical Sciences Review and Research 3(2): 49-54.

[12]. Md Intakhab Alam, Nawazish Alam, Vikramjit Singh, Md Sarfaraz Alam, Md Sajid Ali, et al. (2013) Type, Preparation and Evaluation Of Transdermal Patch: A Review. World Journal of Pharmacy and Pharmaceutical sciences 2(4): 2199-2233.

[13]. Archana K Gaikwad (2013) Reviewed Article, Transdermal Drug Delivery System: Formulation aspects and evaluation. Comprehensive Journal of Pharmaceutical Sciences 1(1): 1-10.

[14]. Y Zhang J Yu AR Kahkoska J Wang J B Buse Z Gu Advances in transdermal insulin deliveryAdv Drug Deliv Rev2019139517010.1016/j.addr.2018.12.006

[15]. P De Vos MM Faas M Spasojevic J Sikkema Encapsulation for preservation of functionality and targeted delivery of bioactive food componentsInt Dairy J2010204292302.

[16]. P Heifer TR Shultz Coupled feedback loops maintain synaptic long-term potentiation: A computational model of PKMzeta synthesis and AMPA receptor traffickingPLoS Comput Biol2018145100614710.1371/journal.pcbi.1006147.

[17]. B Barry EM Aulton Transdermal drug deliveryThe science of dosage forms design, 2nd edn. Harcourt publishersChurchill Livingstone, New York2002499533.

[18]. AC Williams BW Barry Penetration enhancersAdv Drug Deliv Rev201264512818.

[19]. P Kumar C Sankar B Mishra Delivery of macromolecules through skinIndian Pharm200453717.

[20]. LC Ng M Gupta Transdermal drug delivery systems in diabetes management: A reviewAsian J Pharm Sci2020151132510.1016/j.ajps.2019.04.006.
[21]. J Gupta A Thakur S Thakur Transdermal drug delivery system of Metformin Hydrogen Chloride using Two Different Polymeric CombinationsInt J Heal Biol Sci20192415.
[22]. SG Danby Biological Variation in Skin Barrier Function: From A (Atopic Dermatitis) to X (Xerosis)Curr Probl Dermatol201649476010.1159/000441545.
[23]. Dhiman Sonia (2011) Transdermal Patches: A Recent Approch To New Drug Delivery System. International Journal of Pharmacy and Pharm 3(5).