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A Review on Transdermal Patches of Antidiabetic Agent

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ABSTRACT:

Approximately 74% of drugs consumed today orally are proven to be ineffective. To enhance these characters, TDDS was created. Transdermal drug delivery devices are one of the most significant innovative drug delivery techniques. Transdermal Drug delivery system is also known as 'Transdermal patches'. Drug application to the skin is crucial for both local and systemic effects. Transdermal drug delivery systems' primary goal is to deliver medication into the bloodstream through the skin at a predefined pace with little inter- and intrapatientvariation. Drug distribution via the skin to have an overall impact without causing changes in the drug's plasma concentration. It is a painless method of medication delivery. The advantages of transdermal medication administration over injectable and oral routes include improved patient compliance and the avoidance of first pass metabolism. Polymer matrix, pressure-sensitive adhesives, release linear, permeation enhancers, backing laminate, additional excipients like plasticizer, and solvents are some of the fundamental parts of TDDS. Diabetes, a long-term metabolic illness brought on by insulin shortage, is characterized by hyperglycemia, altered protein, carbohydrate, and lipid metabolism, as well as a higher risk of vascular complications. Anti-diabetic medications are a prime choice for transdermal drug delivery systems because to their frequent dosage, substantial first passes metabolism, and variable bioavailability. Biguanides, meglitinide, sulfonylureas, and DPP4 inhibitors are only a few of the anti-diabetic transdermal patches that are now offered on the pharmaceutical market. By acting as a barrier, the stratum corneum restricts the amount of material that may pass through the skin, but these restrictions can be removed via permeation-enhancing procedures. A transdermal patch's quality, size, onset and duration, adhesive property, thickness, weight, moisture content, and homogeneity are all examined during characterization.

Keyword- Transdermal Drug Delivery system, diabetes mellitus, Antidiabetic drugs, Skin, Transdermal Patches.

INTRODUCTION

One of the finest for delivering new medication is transdermal administration.Compared to more traditional delivery techniques like oral and intravenous administration, transdermal medication delivery offers additional benefits. The commonly used transdermal medication administration method, which eliminates gastro intestinal toxicity and is easy and painless, employs a patch to transfer the therapeutic material via the skin. [1]

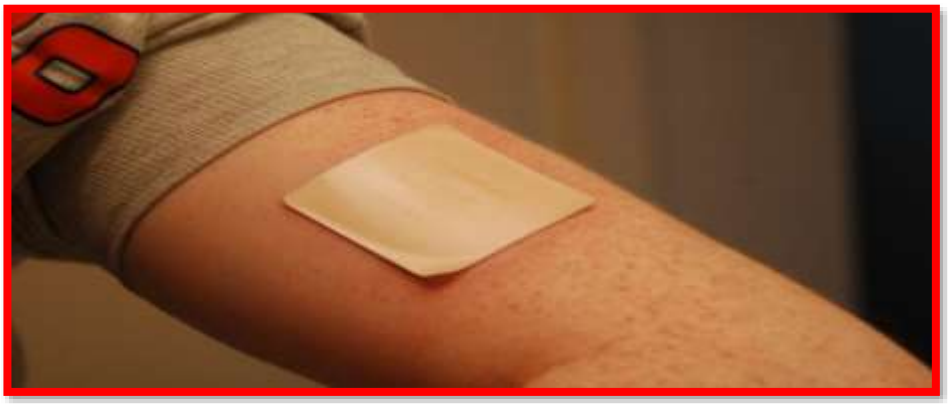

Fig. 1 Transdermal Patch

Transdermal medication delivery systems provide a few benefits over traditional drug administration techniques that encourage patient compliance. Transdermal patches have seen tremendous growth in recent years due to their non-invasive nature, ease of application and removal, PH-determined rate of drug permeation, increased bioavailability of drug, and decreased hepatic metabolism. As a result, this system is best for systemic drug delivery over long periods of time, such as 24 hours. [2]

Advantages of Transdermal Drug Delivery System -

- First pass drug metabolisms are avoided.
- It is possible to self-medicate.
- The dosage quantity is reduced, which enhances patient compliance.[3]

Disadvantages of Transdermal Drug Delivery System -

- Before deciding to design a transdermal product, it is important to thoroughly consider clinical necessity.
- The skin's ability to act as a barrier varies from one spot to another on an individual, from person to person, and with age.
- Localized erythema, irritation, and edema can be brought on by the medication, the adhesive, or another excipient in the patch formulation. [4]

Applications of Transdermal Patches -

- Transdermal nicotine patches, which administer nicotine in regulated doses and support quitting smoking.
- Nitro-glycerin patches are occasionally applied. a medication that is prescribed to treat angina.
- Clonidine, an antihypertensive drug, and ketoprofen. Transdermal patches for non-steroidal, anti-inflammatory drugs are also increasingly accessible.
- The transdermal administration method for an initial antidepressant using the MAOI selegiline. [5]

ANTIDIABETIC DRUGS –

1] METFORMIN – (BIGUANIDES)

Transdermal patches of MFH were made utilizing various polymer ratios, such as PVP K30 and E50, using solvent evaporation process in cylindrical, glass moulds with both sides open. [6]

2] GLIMEPIRIDE – (SULFONYLUREAS)

Glimepiride is a third-generation oral sulphonyl urea medication that is regularly used to type 2 diabetes patients. The solvent casting process is used to create transdermal glimepiride patches. Polysorbate 60 and eudragitE-100 are used to improve penetration. Dibutyl phthalate, a plasticizer, aids in increasing penetration. [7]

3] REPAGLINIDE – (MEGLITINIDE)

Transdermal patches for repaglinide were developed to prolong medication release, improve bioavailability, and raise patient compliance. By adjusting the grades of HPMC and the concentration of PVP K30 using the solvent casting process, several formulations were created. [8]

4] VILDAGLIPTIN – (DPP4 INHIBITOR)

Vildagliptin has unique physiochemical characteristics, including a low water solubility, a tiny molecular mass, and a reasonable melting point, which indicate to the possibility of skin delivery. Vildagliptin transdermal patches were created utilising almond oil as a penetration enhancer and powdered aloe Vera gel as a polymer. patches made using the solvent evaporation method. [9]

ANTIDIABETIC ACTION AND MECHANISMS -

Other unique mechanisms can also be used to lower blood sugar levels Skeletal tissue is a key organ for removing and absorbing glucose among them. It may be done using two different techniques. Akt and phosphatidylinositol-3-kinase (PI3-K) facilitate the movement of glucose from the intracellular pool to the plasma membrane.[10]

SKIN PATHWAY FOR TRANSDERMAL DRUG DELIVERY SYSTEM -

When a medicine is put to the skin's surface, there are several different ways that it might penetrate the skin. Drugs can enter the body either trans epidermally (through the stratum corneum) or transapically (via the appendages).(I)There are two distinct ways to penetrate the corneum: I the transcellular route, which alternates between the corneocyte and the lipid lamellae, and (II) the convoluted road along the lipid lamellae (intracellular route).It is generally acknowledged that the intracellular pathway is the most common way to penetrate the stratum corneum. This is mostly due to the highly cross-linked cornified membrane that covers the keratinocytes.[11]

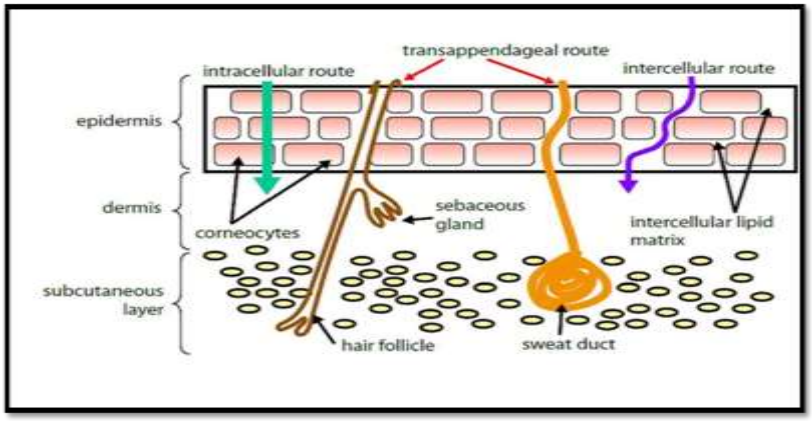

FIG 2. SKIN PATHWAYS FOR TRANSDERMAL DRUG DELIVERY SYSTEM

5] COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEM –

a) Polymer Matrix / Drug Reservoir -

The medication is dispersed in a synthetic polymer base that is either liquid or solid to create the polymer matrix, or drug reservoir. It should be chemically and biologically compatible with the medicine as well as other system components like the penetration enhancer.

Polymers used in transdermal drug delivery system -

i) Natural polymers e.g. gelatine, wax, gum, etc.

ii) Synthetic elastomers e.g. polybutadiene, hydrin-rubber etc.

iii) Synthetic polymers e.g. polyvinyl chloride etc.

b) Pressure Sensitive Adhesive (PSA) -

It aids in improving the transdermal patch's skin-surface adhesion. Without leaving behind any residue, it may be removed from the smooth surface with ease.

i) Polyacrylate.

ii) Polyisobutylene.

iii) Silicon based adhesive.

c) Release liner –

This is the main type of packaging that may safeguard the patch while being applied. It is composed of a base layer, which may be –

i) Non-occlusive (e.g. paper fabric) OR

ii) Occlusive (e.g. polyethylene, polyvinylchloride). It is made up of silicon or Teflon.[3]

d) Drug -

Careful consideration should be given to the medication selection in order to successfully build a transdermal drug delivery system.

The following are some of a drug's preferable characteristics for transdermal distribution.

Physicochemical properties:

1) The drug's molecular weight should be less about 1000 Daltons.

2) The medication should bind to both lipophilic and hydrophilic patches.

Biological properties:

1) The drug's half-life (t1/2) should be short.

2) Skin irritation or an allergic reaction must not be brought on by the medicine.

e) Permeation Enhancer -

A chemical known as a permeation enhancer temporarily lowers the skin's impermeability. By altering the way the skin functions as a barrier to the flow of the intended penetrant, these substances operate to make the skin more permeable.[12]

f) Baking Laminate -

This safeguards the patch from the outside environment. They must be resistant to chemicals. They won't permit components in patches to permeate them. Their elasticity, suppleness, and tensile strength are ideal. Polyethylene, vinyl, etc. [13]

g) Other excipients like plasticizer and solvents -

1|) Solvents - Chloroform, methanol and dichloromethane.

2) Plasticizer - Plasticizer they are used to provide plasticity to transdermal patch. E.g. PEG, PG.[3]

6] TYPES OF TRANSDERMAL PATCHES –

1) Single Layer Drug in Adhesive -

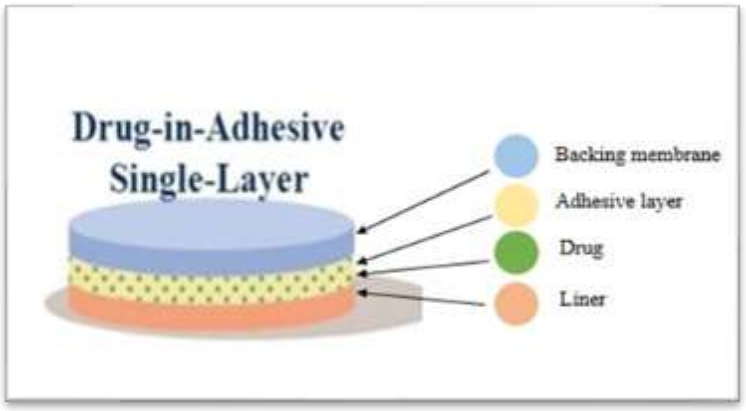

Fig. 3 Single Layer Drug In Adhesive

The incorporation of the medicine directly within the skin-contacting adhesive is what distinguishes the Single-layer Drug-in-Adhesive system. In this transdermal system design, the adhesive not only acts as the basis for the formulation, holding the medicine and all excipients in a single backing sheet, but it also serves as a means of attaching the system to the skin.

2) Multi-layer Drug in Adhesive -

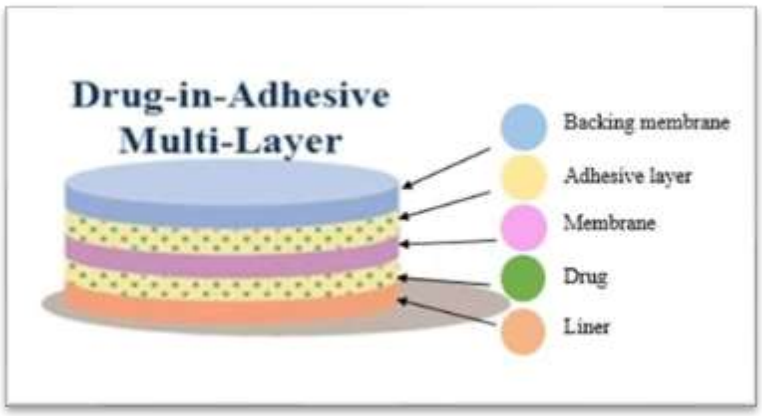

Fig.4 Multi-layer Drug In Adhesive

Similar to the single layer drug in adhesive, the multi-layer drug in adhesive incorporates the medication right into the glue. However, the term "multi-layer" includes the insertion of a membrane between two different drug in adhesive layers as well as the placement of additional drug in adhesive layers beneath a single backing film.

3) Reservoir Drug In Adhesive -

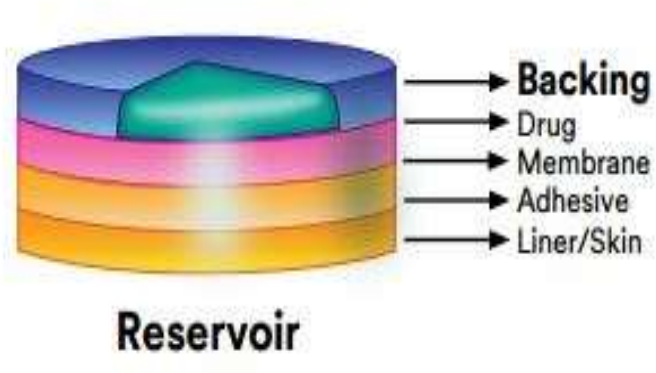

Fig. 5 Reservoir Drug In Adhesive

The addition of a liquid compartment containing medication solution or suspension that is separated from the release liner by a semi-permeable membrane and adhesive defines the reservoir transdermal system design.

4) Drug Matrix In Adhesive -

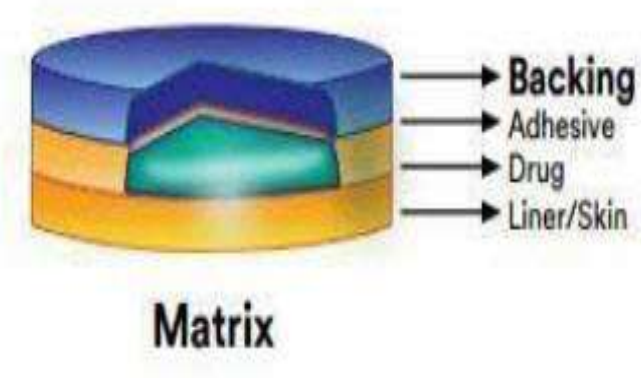

Fig. 6 Drug Matrix In Adhesive

The addition of a semisolid matrix holding a medication solution or suspension that is in direct contact with the release liner characterises the matrix system design.[14]

MAIN INGREDIENTS USED FOR THE PREPARATION OF TRANSDERMAL DELIVERY SYSTEM -

- **Liners -** These shield the patches during storage, but they need to be taken off before usage.
- **Adhesive-** The patch's component parts were held together with the help of it. The skin patch is applied in addition.
- **Membrane-** The membrane patches regulate the multi-drug layer's release. Alternatively known as the permeation enhancer.
- **Drug-** Direct contact between the releasing liner and the drug reservoir.
- **Baking-** Guards against environmental damage.[15]

Drug and Excipient - (Material used in the present investigation)

Table 1: List of material used.[16]

Sr. No	Materials	Purpose
1	Sodium Lauryl Sulphate	Solubilizer
2	Sodium Hydroxide	pH Adjustment
3	Sodium Dihydrogen Phosphate Dihydrate	Buffer
4	Acetone	Solvent
5	Dimethyl Sulfoxide	Permeation Enhancer
6	Triethyl Citrate	Plasticizer
7	PVP K-30	Polymer
8	Eudragit NE 30D	Polymer
9	Anti Diabetic Drug	API

PREFORMULARTION STUDIES –

Pre-formulation tests were conducted to determine a medication's physicochemical properties (TPM) and its compatibility with various excipients before the drug ingredient was formulated into a transdermal patch (dosage form). such as IR and UV spectrometric investigations, solubility, partition coefficient, melting point, and organoleptic qualities.

1) Organoleptic Properties –

Identify the colour, odour, taste, and condition.

2) Determination of melting point –

In this procedure, a little quantity of the drug was deposited in a capillary tube that was closed at one end and placed in Thiele's melting point device. The temperature at which the drug melted was then recorded. Readings in triplicate were averaged.[17]

3) Solubility -

In a solubility research, the drug was tested in several solvents. This might be useful in choosing a solvent that will effectively dissolve the medication and any excipients used in formulations. The pH, ionic strength, temperature, and buffer concentration all affect a drug's solubility.[18]

4) IR spectrophotometric studies -

The infrared spectra of a chemical can reveal the group that that compound belongs to. A small amount of medication was combined with oil, and one drop was then evenly distributed between two KBr pellets. The pellets were put in a holder, and infrared spectra were collected. Different peaks in the spectrum were interpreted to indicate the presence of specific groups in the drug's structure.

6) UV spectrophotometric studies -

These studies serve as an addition to the instruments used to identify drugs. Using a UV visible spectrophotometer to analyse the drug's UV spectrum in various solvents. The acquired spectrum was compared to the reference.[19]

10] METHOD OF PREPARATION OF TRANSDERTMAL PATCHES –

a) Asymmetric TPX membrane method -

A prototype patch may be made for this method, which uses a heat-sealable polyester film (type 1009,3m) with a baking membrane that has a concave of 1 cm in diameter. A TPX poly(4-methyl-1-pentene) asymmetric membrane converts the drug sample before it is distributed into the concave membrane and sealed with an adhesive.

b) Circular Teflon mould method –

In this technique, organic solvent is utilized to dissolve solutions containing polymers in varied ratios. Calculate the drug's concentration after diluting it with half as much of the same organic solvent. Di-N-Butyl phthalate, a sticky substance, is added to the drug solution and dissolved after the enhancer is

first dissolved in the other half of the organic solvent at various concentrations. Aluminum foil lines a custom-made aluminium former, which has cork blocks that fit snugly around the ends to blank them off.

c) Mercury substrate method –

In this procedure, the medication is dissolved in a plasticizer-laced polymer solution. The aforementioned solution should be agitated for 10 to 15 minutes to provide a uniform dispersion before being placed over a mercury surface that has been levelled and covered with an inverted funnel to prevent solvent evaporation.

d) By Using "IPM Membrane" method –

In this technique, the medication is dissolved in a solution of water and propylene glycol that also contains carbomer 940 polymer, and the combination is then agitated for 12 hours using a magnetic stirrer. Triethanolamine is to be added in order to neutralize the dispersion and make it viscous. If the medicine has very poor water solubility, a buffer with a pH of 7.4 can be utilized to create solution gel. The IPM membrane will incorporate the produced gel.

e) By using "EVAC membranes" method –

1% carbo-pol reservoir gel, polyethylene (PE), and ethylene vinyl acetate copolymer (EVAC) membranes can be employed as rate-controlled membranes to produce the target transdermal treatment system. Propylene glycol is used to make gel when the medication is not soluble in water. Drug is dissolved in propylene glycol; carbo-pol resin is added to the aforementioned solution; and the mixture is neutralised with a 5% w/w solution of sodium hydroxide. The medication is applied on a baking sheet, transforming the designated area, in gel form. To create a leak-proof device, a rate-regulating membrane will be put over the gel, and the edges will be heated to seal them.

f) Aluminium backed adhesive film method –

If the loading dose is more than 10mg, the transdermal drug delivery system may result in unstable matrices. The aluminum-backed sticky film approach is appropriate. Because most medications and adhesives are soluble in chloroform, it is the solvent of choice for making the same. In chloroform, the medicine is dissolved, and then adhesive material is added and dissolved in the mixture. Aluminum foil is used to line a custom-made aluminium former, and cork blocks that fit snugly around the edges are used to seal off the ends.[14]

11] CONDITIONS IN WHICH TRANSDERMAL PATCHES ARE USED –

The transdermal patch used when -

1) A patient with dysphagia requests an alternate channel of drug administration since they are unable to take oral medicine owing to intolerable side effects (including constipation).

CONDITIONS IN WHICH TRANDERMAL PATCHES ARE NOT USED –

The use of transdermal patch is not suitable when -

1) a cure for acute pain is desired, transdermal patches are not appropriate.

2) When the dosage needed is equal to or less than 30 mg/24 hours.[11]

12] EVALUATION TEST OF TRANSDERMAL PATCH –

1) Thickness -

A digital micrometer is used to measure the thickness of the drug-loaded patch at various spots, calculating the average thickness and standard deviation for the same to guarantee the produced patch's thickness.

2) Weight Uniformity -

Before testing, the produced patches must be dried at 60°C for four hours. It is necessary to compute the average weight and standard deviation values from the individual weights. [20]

3) Folding Endurance -

The film is folded until it breaks by folding it repeatedly in the same spot. The quantity of folds that the films could withstand at the same location before breaking determined the folding endurance. [19]

4) Percentage Moisture Content -

Weigh each manufactured film individually and place it in a desiccator with fused calcium chloride for 24 hours at room temperature. The films must be reweighed in order to calculate the % moisture content.

5) Percentage Moisture Uptake -

To maintain 84% RH, weighted films are placed in desiccators at room temperature for 24 hours and are submerged in a saturated potassium chloride solution. The film is reweighed after 24 hours, and the aforementioned method is used to calculate the % moisture absorption.

6) Water Vapour Permeability Evaluation -

WVP may be assessed using the foam dressing technique and a natural air circulation oven in place of an air-forced oven. You may determine the WVP by –

Following formula –

$$WVP = W / A$$

Where, WVP is measured in grams per square meter each day.

W is the quantity of vapour that infiltrated the patch, measured in grams every 24-hour period.

A is the exposure sample's surface, measured in square meters.

7) Stability Studies -

In accordance with the ICH guidelines, stability studies must be carried out by holding TDDS samples at 40 0.5°C and 75 5% RH for six months. [20]

8) Adhesive Studies -

PSAs, which are described as adhesives capable of bonding to surface with the application of mild pressure, are used to adhere a TDDS to the skin. The following elements can be used to describe a TDDS's adhesive qualities.

- Peel Adhesion Test.
- Thumb Tack Test.
- Rolling Ball Test.
- Quick Stick Test.
- Probe Tack Test.
- Shear Adhesion Test.

9) In Vitro Drug Release Studies -

There are several ways to calculate the TDDS drug release rate.

- The paddle over disc.
- The cylinder modified USP basket.
- The reciprocating disc.
- Diffusion cell E.g. Franz diffusion and its modification keshary chain cell.

10) In Vitro Skin Permeation Studies -

Typically, in a vertical diffusion cell like a Franz-diffusion cell, permeation tests are carried out by inserting a transdermal patch made of synthetic membrane or rat skin between the donor and reported compartments. The hydrophilic side of the membrane receives the transdermal system before mounting in the diffusion cell with the lipophilic side in contact with the receptor fluid. The receiver compartment is continually swirled at a consistent pace and kept at a certain temperature (about 32 ± 5 °C for skin). Sample examined using a spectrophotometric technique.[21]

MARKETED FORMULATION –

Table. 2 – Examples of marketed transdermal drug delivery system.[16]

Product name	Drug	Manufacturer	Indication
Alora	Estradiol	Thera Tech / Protocol and Gamble	Postmenstrual Syndrome
Androderm	Testosterone	Thera Tech / GlaxoSmithKline	Hypogonadism (male)
Catapres-TTS	Clonidine	Alza/ Boehinger Ingelhein	Hypertension
Climaderm	Estradiol	Ethical Holding / Wyeth- A yarest	Postmenstrual Syndrome
Climara	Estradiol	3M Pharmaceuticals / Berlex Labs	Postmenstrual Syndrome
Combipatch	Estradiol / Norethindrone	Noven, Inc. / Aventis	Hormone Replacement Therapy
Deponit	Nitro-glycerine	Schwarz-Phrma	Angina Pectoris
Duragesic	Fentanyl	Alza/ Janssn Pharmaceutical	Pharmaceutical Moderate / Severe Pain
Estraderm	Estradiol	Alza/Novartis	Postmenstrual Syndrome
Fematrix	Estrogen	Ethical Holdings/Solvay Healthcare Ltd	Postmenstrual Syndrome
Fempatch	Estradiol	Parka-Davis	Postmenstrual Syndrome
Habitraom	Nicotine	Novartis	Smoking Cessation
Minitran	Nitro-glycerine	3M Pharmaceuticals	Angina Pectoris
Nicoderm	Nicotine	Alza / GlaxoSmithKline	Smoking Cessation
Nicotrol	Nicotine	Cygnus Inc. / McNeil Consumers Products, Ltd	Smoking Cessation
Nitrodisc	Nitro-glycerine	Roberts Pharmaceuticals	Angina Pectoris
Nitrodur	Nitro-glycerine	Key Pharmaceuticals	Angina Pectoris
Nuvelle	Estrogen / Progesterone	TS Ethical Holdings / Schering	Hormone Replacement Therapy
Orth-Evra	Norelgestromin / Estradiol	Ortho-McNeil Pharmaceuticals	Birth Control

CONCLUSION –

A brief analysis of the various diabetes medication showed that transdermal delivery significantly increases both bioavailability and patient compliance. However, one drawback is that not all anti-diabetic medications can be administered via transdermal delivery because they have unique physiochemical

characteristics that must be suited to permeate skin. A successful transdermal drug delivery system also requires careful consideration of the drug, the polymer, and other addictive factors.

15] REFERENCE –

1. Prashant Narayan Solanke, Abdul Wahid Ambekar, Satyam Chemate, Formulation, development and characterization of transdermal drug delivery system for antidiabetic drug, Asian Journal of Pharmacy and Pharmacology 2018; 4(5):668-672.

2. Chakshu Bhatia, Monika Sachdeva and Meenakshi Bajpai, formulation and evaluation of transdermal patches of pregabalin, Bhatia et al., IJPSR, 2012; Vol. 3(2): 569-575.

3. Nidhi Sharma HIMT College of Pharmacy, Greater Noida, India, A Brief Review on Transdermal Patches, Organic and Medicinal Chemistry International Journal ISSN 2474- 7610.

4. Dhaval J. Patel, Ajay M. Vyas, Sanjesh G. Rathi, Shrenik K. Shah, Formulation and Evaluation of Transdermal Patch of Apixaban. Department of Pharmaceutics, Saraswati Institute of Pharmaceutical Sciences, Dhanap. Gandhinagar, Gujarat, INDIA, J. Pharm. Sci. Rev. Res., 69(2), July - August 2021; Article No. 09, Pages: 57-63.

5. Audumbar Digambar Mali, Ritesh Bathe and An updated review on transdermal drug delivery systems, Audumbar Digambar Mali et al /International Journal of Advances in Scientific Research 2015; 1(06): 244-254.

6. G. Bhagyeshwar, B. Ramu, Bigala Rajkamal, formulation and evaluation of transdermal patches of metformin hydrochloride, Bhagyeshwar et al, WRJPT, 2017, 2(4): 1-20.

7 Mounika P, Rinkumathappan, Sukriti Vishwas, The Individual Effect of Surfactants on The Penetration of Glimepiride Transdermal Patches Using Dibutyl pathalate as a Plasticizer, Department of Pharmaceutics Gautham College of Pharmacy, Bangalore – 560032.

8. Shailesh T. Prajapati, Charmi G. Patel, and Chhagan N. Patel, Formulation and Evaluation of Transdermal Patch of Repaglinide, International Scholarly Research Network ISRN Pharmaceutics.

9. Renuka Namdeo, Mukesh Kumar Patel1, Ashish Manigauha, Arun Pandey, Research article, Formulation and evaluation of transdermal patch of vildagliptin, International Journal of indigenous Herbs and Drugs ISSN-2456-7345.

10. R Vijayaraj and Swaranakala. Review article “Antidiabetic Drugs: Mechanisms and Their Effects". Acta Scientific Medical Sciences Special Issue 1 (2019): 11-13.

11. D. Prabhakar, J. Sreekanth, K.N. A Jayaveera, review A Review Article on Transdermal patches: A review, Journal of Drug Delivery & Therapeutics; 2013, 3(4), 213-221.

12. P. Palanisamy, B. Jaykar, B.S. Venkateswarlu, R. Margret Chandira, and Suriyan. A review Article: A Review on Transdermal Drug Delivery System. Indian Journal of Natural Sciences ISSN: 0976 – 0997.

13. Chetan Ghulaxe, Mousumi Karpillai, Sujit Pillai, Pankaj Kushwah, Ranu Mansare. Review article: Review on Transdermal drug delivery systems. World journal of pharmaceutical and medical research. vol, 2017,3(8),63-71.

14. Virendra Yadav, Review Article: Transdermal drug delivery system review. international journal of pharmaceutical sciences and research Yadav, IJPSR, 2012; Vol. 3(2): 376-382.

15. Chetan Ghulaxe, Rameshwar Verma, A review on transdermal drug delivery system, The Pharma Innovation Journal 2015; 4(1): 37-43.

16. Mayank P. Patel, M. M. Gupta1, Transdermal Patch of Anti-Diabetic Drug, The pharma innovation- Journal, ISSN: 2277- 7695.

17. Dharmesh Trivedi, Anju Goyal, Seema V. Joshi, Reformulation studies formulation of the Transdermal patches of the drug, may 2022.

18. Pallavi M. Chaudhari, Aarti V. Paithankar, formulation and optimization and evaluation of transdermal patches of vildagliptin for treatment of diabetes mellitus ,1Associate Professor, Department of Pharmaceutics.

19. Poojashree Verma, Deepika Bairagi, Aswin Somkuwar, Mukesh Mehra and Mahavir Chhajed, Formulation and Evaluation of Transdermal Patch of Glibencl-amide, International Journal of Pharmacy & Life Sciences Verma et al., 11(7):6724-6737, 2020.

20. Waghulde S., Naik P.P. Gorde N. Juvatkar P. Shirodkar P.Y. Kale M.K. Review article: Development, Recent Inventions and Evaluation Techniques of Transdermal Drug Delivery System - A Review Article.et al / Int. J. Pharm. Phytopharmacology. Res. 2013; 3 (2): 152- 160.

21] Bhairam Monika, Roy Amit, Bahadur Sanjib, Banafar Alisha, Patel Mihir, Turkane Dhanushram. Review article: Transdermal Drug Delivery System with Formulation and Evaluation Aspects: Overview. review article. Research J. Pharm. and Tech. 5(9): September 2012; Page 1168-117.