WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Transdermal Drug Delivery Systems – Transdermal Patches

Sonali Santosh Borde [a], Sunanda Bhavrao Kharat [b], Sonali Achyut Todkar [ab*], Ayodhya Narayan Ghandge[ab**], Sujata Sahebrao Bobade[ab]***

[a,b] *Nandkumar Shinde College of Pharmacy, Vajapur, Dr. Babasaheb Ambedkar Technological University, Lonere, Maharashtra, India.*

ABSTRACT:

Transdermal drug delivery systems are among the best administered drug delivery systems. Transdermal drug delivery systems have many advantages, such as improved bioavailability and therapeutic effect, reduced side effects and dosing frequency. The drug penetrates the skin in three different ways. Generally, these are intracellular and intracellular appendages. Transdermal patches are currently used. Transdermal patches are adhesive drug patches that are applied to the skin and release the drug into the systemic circulation over an extended period of time. Transdermal patches are mainly used for new drug delivery systems.

Keywords: *Transdermal Systems, Transdermal Patches, Adhesive Medical Patches, Laminate Backings, etc*.

1. INTRODUCTION: -

Over the past few years, there has been a renewed interest in developing novel drug delivery systems for existing molecules. The development of new drug delivery systems for different types of molecules not only improves drug performance in terms of efficacy and safety, but also improves patient compliance. A transdermal drug delivery system for topical application of drugs using a variety of transdermal drug patches. The transdermal patches improve bioavailability and better patients' compliance and easy to use [pawan Jalwal et al 2010], [Andrew J Carmichael 1994].

Transdermal patches are medicated adhesive which, when placed on skin using patches, the specific dose of drug through the skin into blood stream. The transdermal drug delivery approach has several advantages: it can avoid the difficulties associated with the oral administration of the drug [Jinsha P et al2018],[1Vaibhav Rastogi et al 2012].Different sizes of patches or transdermal patches are available which contain more than one ingredient and when they are applied on the skin, active ingredients are delivered into the systemic circulation passing via the skin barrier. Transdermal patches have the capacity to contain high doses of drug inside them and retain on the skin for a tiring period of time and enter into the blood by diffusion process in controlled release manner [Nidhi Sharma 2018],[Shubham Banerjee et al 2014]

For an oral drug delivery system, patients often forget to take the medicine; hence causing the patient's medication adherence and poor patient compliance is obtained due to some difficulties like swallowing pills for several days, causing irritation to prevent such problems. Transdermal patches are applied only to the skin and are easy to use [Kamal Saroha Bhavna Yadav et al] [David Bird et al 2020]. Transdermal drug delivery systems are used for a variety of skin conditions, as well as for the treatment of angina pectoris, pain, smoking cessation, and neurological disorders such as Parkinson's disease [Nidhi Sharma 2018], [Pwan Jalwal 2010].

2. ANATOMY AND PHYSIOLOGY OF SKIN

Adult skin with an average surface area of 2 cm2. Human skin consists of three separate but interdependent tissues: epidermis, dermis and subcutaneous tissue.

2.1 Epidermis:

It is composed of two parts like the middle layer of the epidermis, and the thickness varies according to the number of cells and the cell layer of the dermis. The skin, also called the stratum cornea, is dry with a thickness of about 10 am, but swells several times when it gets damp. 8mm in the palm, it consists of the clear layer, the granular layer, the spinouts layer, and the base of the foot [Nidhi Sharma 2018], [Eseldin Keleb et al 2010], and [Gaurav Upadhyay et al 2014].

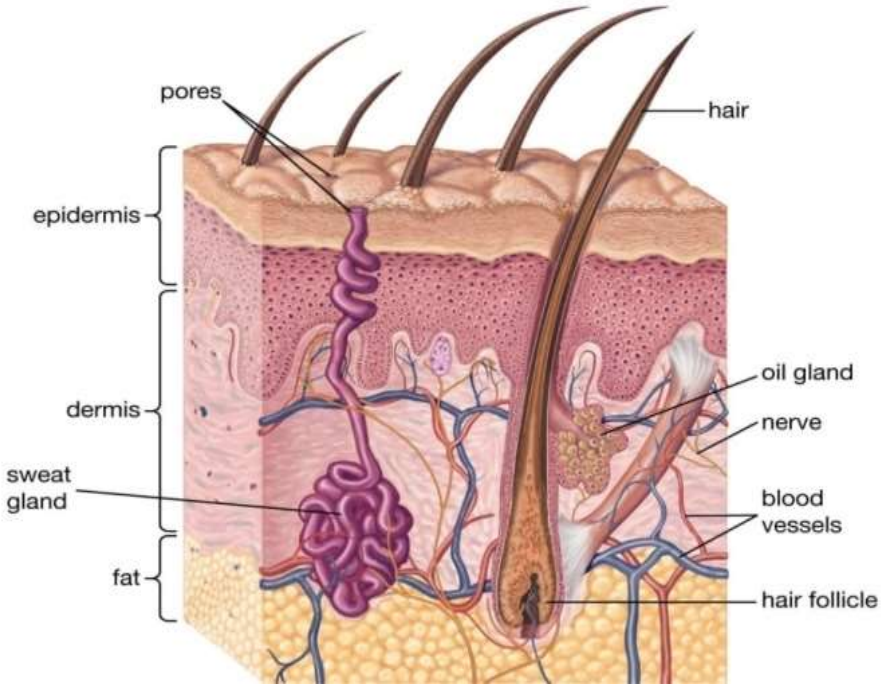


Fig 1. Anatomy of the skin

2.2 Dermis:

The dermis is a layer 3 to 5 mm thick and consists of a matrix and connective tissue that contains blood vessels, lymph vessels and nerves.

2.3 Subcutaneous tissue:

Subcutaneous tissue and subcutaneous fatty tissue support the dermis and epidermis. Serves as a warehouse. This layer helps regulate temperature and provides nutritional support and mechanical protection [Nikhil Sharma et al 2011], [Elesdin Keleb 2010] [Dr Prabhakar et al 2013].

3. ADVANTAGES

- Appropriate for drug candidates with short half-lives.
- No first pass metabolism
- Reduced dosing frequency
- Reduced plasma drug concentration variability
- Increased patient compliance
- Minimized side effects Transdermal Drug Delivery System (PAS)[Kamal Saroha Bhavna Yadav et al],[S Lakshmi Savitri et al 2021]

4. COMPONENTS

a) Drug

b) Drug reservoir

c) permeation enhancer[Mutalik S et al 2005],[Jhawat VC et al 2013]

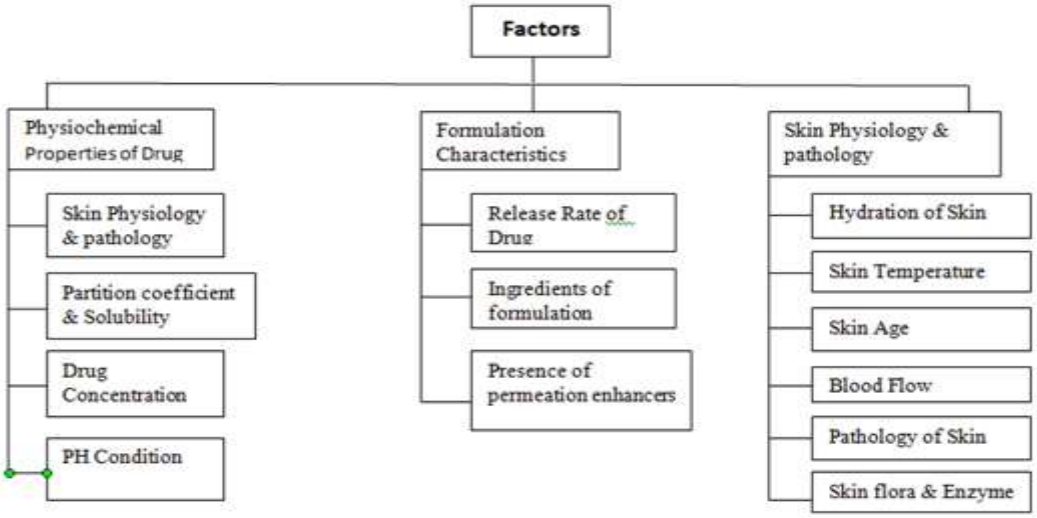
d) backing laminat

e) pressure sensitive adhesive(PAS)

f) Release films

g) Other excipients such as plasticizers and solvents.[Pawan Jalwal et al 2010][Andrew J Carmichael et al 1994].

5. FACTOR AFFECTING TRANSDERMAL DRUG DELIVERY SYSTEM



Factors of TDDS

6. TRANSDERMAL PATCH:

Transdermal patches are a mediated adhesive patch containing medication which goes into systemic circulation through the skin [Jinsha P et al 2018].

6.1 Need for transdermal patch:

Transdermal drug delivery system is the delivery of medicine through the dermal route of administration by first gastrointestinal complications, oral incompatibility of various drugs. This route of administration of drug shows better plasma concentration with enhanced bioavailability compared to other formulations containing same impediment. The Patches containing more than one medicament are very useful for managing different diseases and achieving best outcome with patient care oriented therapy. The major side effects such as lacto acidosis, drug toxicities can be reduced through using transdermal patches [S Lakshmi Savitri et al 2021], [Ashish Rawat et al 2016].

7. BIOPHARMACEUTCAL PARAMETERS OF DRUG SELECTION FOR TRANSDERMAL PATCHE

a. Doses should be low. low i.e.<20mg / day
b. Half life should be 10 hr or less
c. Molecular weight should be <400
d. Partition coefficient should be log P(octane -water) between 1.0 to 4
e. Skin permeability coefficient should be<0.3×10-3cm/ h
f. Drug should be non irritating and non sensitizing to skin
g. Oral bioavailability should be low
h. Therapeutic index should be low [4Kamal Saroha Bhavna Yadhav et al], [Richard H Guy 2010]

8. APPROACHES USED IN DEVELOPMENT OF TRANSDERMAL PATCHES: -

There are four main approaches for transdermal patch development is as follows

1 System with membrane retardant
2 diffusion controlled adhesion system
3 Matrix dispersion

4 Micro reservoir system

8.1 System with membrane retardant:

In this case the drug reservoir is fully encapsulated 4; end Shallow compartment membrane retardant system molded from drug impermeable metal plastic laminates and rate controlling polymer membranes. In drug reservoirs, drug solids are dispersed in a solid polymer matrix or suspended in a viscous liquid medium that is difficult to leach. Silicone fluid [Kamal Saroha et al], [Vaibhav Rastogi et al 2012]. The rate controlling membrane can be, for example, a micro porous or non-porous polymeric membrane's. Ethylene-vinyl acetate copolymer, drug skin layer, and compatible hypoallergenic adhesive polymers can be applied to the outer surface of the polymer membrane to achieve intimate contact of the skin surface and TDDS [Pawan Jalwal et al 2010], [S Lakshmi savitri et al 2021], [Beverley J Thomas et al 2004].

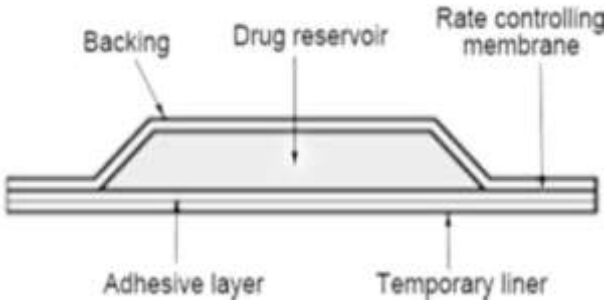


Fig 2: system with membrane retardant.

8.2 Diffusion Controlled Adhesion System:

This is the simplest version of a membrane drug delivery system. This system creates a drug reservoir by Directly dispersing a drug in an adhesive polymer, then casting a solvent onto a flat sheet of metal-plastic substrate that is impervious to the drug, and applying a drug adhesive to form a thin drug storage layer. A layer of non-drug rate-controller adhesive polymer of constant thickness is applied over the storage layer [Beverley J Thomas et al 2004, [Jhawat VC et al 2013]. Medicinal patches can be single or multi-layered. Multilayer systems differ from single layer systems in that they add another layer of drug to the adhesive, usually separated by a membrane. The pharmacological properties of the adhesive patch make it easy to remember to apply the patch once a week and it can contribute to improved patient compliance by improving cosmetic acceptance and adhesion.

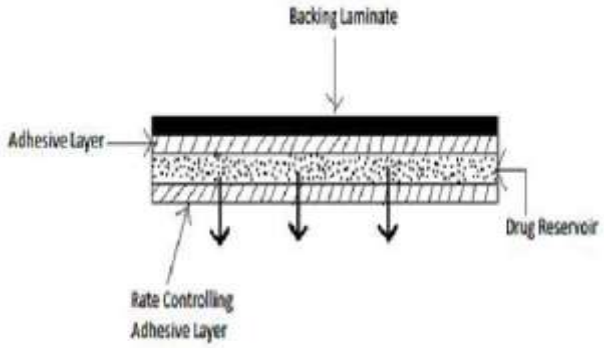


Fig. 3 Adhesive Dispersion Controlled System

8.3 Matrix Dispersion:

Here, a drug reservoir is formed by uniformly dispersing drug solids in a hydrophilic or lipophilic polymer matrix, and then the drug polymer is molded into a disc shape with a certain area and thickness. It adheres to the occlusal base plate on the disc surface, and the adhesive polymer is distributed around the circumference to form an adhesive rim band around the disc. The advantage of the Matrix Patch is that there is no dose dumping, the polymer matrix is directly exposed to the skin, and there is no adhesive interference [Kamal Saroha Bhavna Yadav et al], [Gaurav Upadhyay et al 2014].

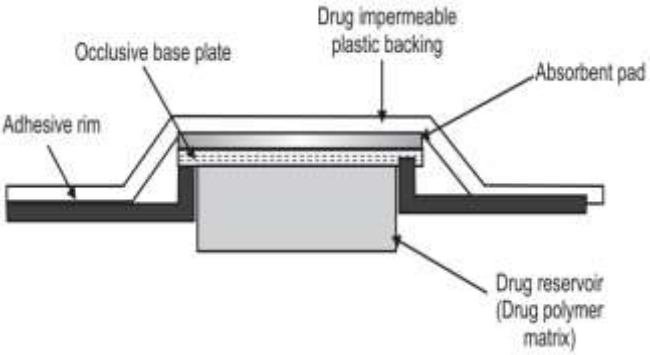


Fig.4 Matrix Dispersion

8.4 Micro reservoir system:

Considered a combination of collector type and matrix variance. At the same time, the drug reservoir is formed by first suspending the drug solids in an aqueous solution of a water-soluble polymer and then dispersing the drug suspension in a homogeneous lipophilic polymer under high mechanical shear to form indelible microspheres of the drug. Reservoir. This dispersion is instantly stabilized by cross-linking the polymer chains to produce drug disks with consistent surface area and thickness [Himanshi Tanwar et al 2016], [Ch Nagadev et al 2020].

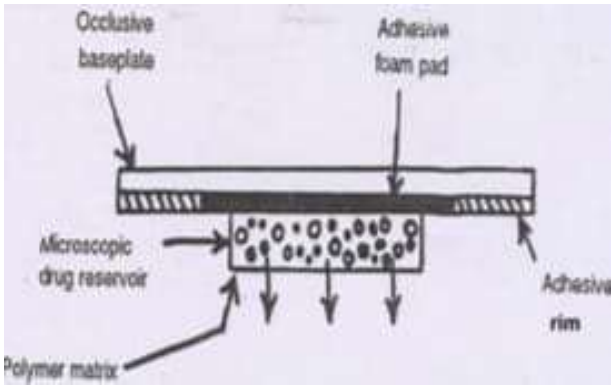
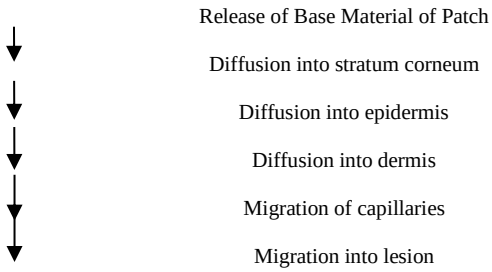


Fig. 5 Micro Reservoir System

9. DRUG AND CLINICAL USES OF TRANSDERMAL PATCHES ON THE CURRENT MARKET.

Drug	Clinical uses	Product name
Clonidine	High blood pressure	Cat après-TTS
Estradiol	Menopause	Estraderm
Estradiol/levonorgestrel	Menopause	*Climara Pro*
Estradiol/norethidrone	Menopause	Combipatch
Fentanyl	Chronic pain	Duragesic
Fentanyl hcl	Postoperative pain	Ionsys
Lidocaine	Pain relief	Lidoderm
Lidocaine/ tetracain	Pain relief	Synera
Methylphenidate	ADHD	Daytrana
Nicotine	Smoking cessation	Nicoderm
Nitroglycerin	Angina pectoris	Transderm-Nitro
Norelgestromin	Contraception	Ortho Evra
Oxybutynin	Overactive bladder	Oxytrol
Rotigotine	Parkinson’s disease	Neupro
Rivastigmine	Dementia	Exelon
Selegiline	Depression	Emsam
Scopolamine	Motion sickness	Transderm-Scop
Testosterone	Testosterone low level	Testoderm

10. MECHANISM OF TRANSDERMAL DRUG PENETRATION OF PATCH



11. TRANSDERMAL PATCH EVALUATION

11.1 Physicochemical Evaluation:

Thickness: The thickness of the transdermal patch is measured at three different points on the patch using a moving microscope, dial indicator, screw indicator, or micrometer. The patch thickness is then calculated as the average of the three measurements. Patches of the same thickness have the same thickness throughout[Kamal Saroha et al],[Chanchal Tiwari et al 2022],[ANJALI V Patel et al 2018]. It can be calculated for thickness variation within and between sections.

Weight uniformity: Patches are dried at 60 °C before weighing. Three patches were cut into 1 cm2 pieces and weighed to evaluate the weight uniformity of the transdermal patch, and then the weight deviation was evaluated.Calculate the patch weight by taking the average of the three values. A person's weight should not deviate significantly from the average weight[Jalawat VC et al 2013].

Folding strength: Fold strength is determined by gradually folding the patch/film strip in the same location until it has been torn or folded up to 300 times. The strength of a patch when folded is determined by the number of times it can be folded without tearing[Mutalik S et al 2005]. Fold strength helps determine the flexibility of a transdermal patch. Strength helps determine the flexibility of a transdermal patch

Drug content: Dissolve films of desired area and weight using an appropriate solvent such as methanol or pH 7.4 phosphate buffer, then filter. After appropriate dilution, measure the drug content using a standard curve by UV or HPLC.

Moisture percentage: . Separately weighed patches are stored for 24 hours at room temperature in molten calcium chloride desiccators to determine moisture percentage. Patches are weighed again after 24 hours and moisture percentage is determined by the formula below

Moisture Percentage = (start weight - final weight/final weight) x 100

Water Absorption Percentage: After leaving the weighed film in a desiccator for 24 hours, it is exposed to 84% relative humidity using potassium chloride. As soon as the weight of the film has stabilized, reweigh the film [Chanchal Tiwai et al 2022], [Audumbar Digmbar Mali 2015].

Percent Water Absorption = (final weight - start weight/start weight) x 100

Shear Adhesion Test: This test evaluates the cohesive strength of an adhesive polymer. The patch with the adhesive was placed on a flat surface and then the required weight was suspended straight from the patch. The shear adhesion of a patch is determined by the time it takes to remove the patch from the surface [Sajid Ali et al 2015], [David Bird et al 2020].

Peel Adhesion Test: This test is used to calculate the force required to remove a patch from a surface. Place the patch using the surface of the grater, then drag it 180 degrees away. Measure the force required to remove the patch. Rolling ball adhesion test. In this test, a 7/16-inch-diameter steel ball is rolled down and tilted, and then the upward-facing patch is placed horizontally on the bonding surface.

Stability Study: Stability studies are conducted to determine if the patch is viable and how long it will be vailable. Because the drug gradually becomes an unstable patch, stability is tested for 6 months at 40 °C/75% relative humidity [S Lakshami savitri et al 2011], [Beverley J Thomsan 2004], [Jhawat VC et al 2013], per ICH recommendations. Sample is collected.

11.2 In vitro studies

In vitro release studies: -The amount of drug that can be absorbed into the systemic pool is highly dependent on the drug released from the polymeric transdermal membrane. Mechanism and kinetics of drug release are two characteristics of dosage forms that play an important role in explaining the dissolution profile of drugs in controlled release dosage forms and thus there in vivo action. Many mathematical models have been developed to describe the dissolution kinetics of drugs in controlled release drug delivery systems [Kamal Saroha et al , [Jain N.K 2002]. E. Higuchi, First order, Zero order and Pappas and Korsenmeyer models. Dissolution data are consistent with these models and are best suited to elucidate drug release mechanisms. The paddle plate over disk method (USP Apparatus 5) is identical to the USP paddle meter. The paddle disk method combined with a 32 degree Celsius ± 5°C watch glass and screen sandwich assembly is considered the preferred method. It is simpler, more convenient, and experimentally shows nearly

identical release profiles compared to other, more complex methods. This method is similar to the USP Dissolving Basket except that the system is adhered to the surface of a hollow cylinder in a 32 ± 5°C environment. . The reciprocating disk method (Device 7 USP) is a device that can be used in a low-concentration drug delivery system by attaching a patch to a holder and vibrating a small amount of medium. The vane extraction method can also be used. Common cells include common Franz cells and variants of Keshari-Chien cells [Chanchal Tiwari et al 2022], [Anjali V Patel et al 2018], and [Mutalik S et al 2005]. In this method, a transdermal system is placed between the recipient and donor diffuse cell compartments.

Transdermal systems are receptor fluids (egg drug solutions). Agitation speed and temperature are kept constant. The entire assembly is kept on a magnetic stirrer and the solution in the receptor compartment is continuously stirred throughout the experiment using magnetic beads. At predetermined intervals, the receiving fluid is removed for analysis and replaced with an equal volume of fresh receiving fluid [Jinsha P et al 2018], [Nikhil Sharma et al 2011], [Jhawat VC et al 2013]. Drug concentrations are determined by appropriate analytical methods. Ideally, the pH of the dissolution medium should be adjusted to pH 5-6 to reflect the physiological state of the skin. For the same reason, the test temperature is usually set to ±32 °C (temperatures can be higher if the skin is closed). Peru considers 100 rpm to be a typical mixing speed, and patch aliquots can also be tested. If cleavage of the patch is confirmed and does not affect the release mechanism, the latter may be a suitable means to achieve the immersion state. The dissolution data generated are fit to a mathematical model to determine the release mechanism [Jain N K 2002].

11.3 In vivo study

Animal Model - Small animal studies are preferred because human studies require significant time and resources. Mice, hairless rats, hairless dogs, hairless rhesus monkeys, rabbits, and guinea pigs are the most commonly used animal species for testing transdermal drug delivery systems. Numerous studies have shown that hairless animals are preferred over furry animals both in the laboratory and under natural conditions [Kamal Saroha Bhavana Yadhav], [Jhawat VC 2013], and [Mutalik s 2005]. One of the best models for analyzing transdermal drug distribution in humans is the rhesus monkey.

Human model - The application of the patch to human volunteers resulted in a collection of pharmacokinetic and pharmacodynamic data at the end of the transdermal device development process. Clinical trials have been conducted to assess the effectiveness, hazards, side effects, patient compliance, and other factors. Faze me clinical trials are used to assess safety largely in volunteers, whereas phase II clinical trials are intended to assess safety and efficacy in patients over the short term. While phase IV trials during post-marketing surveillance are conducted to detect adverse drug reactions, phase III trials demonstrate the safety and efficacy of marketed patches in a vast number of patient populations [Chanchal Tiwari et al 2022], Jain N.K 2002].

CONCLUSION: -

Orally administered pharmacologically active ingredients or drugs cause various problems such as poor patient compliance when taking pills for several days, and may cause gastric irritation due to drug metabolism during the first passage through the skin. This happens to avoid these problems. The drug delivery system is one of the best systems in which a transdermal patch delivers a drug to the systemic circulation through a controlled release method through the skin barrier for a long period of time to improve the therapeutic effect and bioavailability and reduce side effects.

ACKNOWLEDGEMENT: -

In this review all authors are equally contributed all authors are declared that there is no conflict of interest regarding the publication of this paper and no any funding authority.

REFERENCES: -

1) Nidhi Sharma; Review on transdermal drug delivery system ;Organic and Medicinal Chemistry International Journal 7(2),58-62,2018.

2) Pawan Jalwal*,Anju Jangra Lalita Dahiya,Yashpal Sangwan, Rajiv Saroha; A REVIEW ON TRANSDERMAL PATCHES Pharma Research · January 2010 139-149.

3) Jinsha P ,Manas Joshi, Sujith Varma.K*; Formulation and Evaluation of Matrix Transdermal Patch Containing Alendronate Sodium for Improving Patient Compliance; International Journal of Pharma Research - Volume 9 July - December 2018, 74-84.

4) KAMAL SAROHA, BHAVNA YADAV*, BENIKA SHARMA; TRANSDERMAL PATCH: A DISCRETE DOSAGE FORM; International Journal of Current Pharmaceutical Research; Vol 3, Issue 3, 201,98-108.

5) NIKHIL SHARMA1, GETA AGARWAL2, A. C. RANA1, ZULFIQAR ALI BHAT3, DINESH KUMAR; A Review: Transdermal Drug Delivery System: A Tool For Novel Drug Delivery System; Int. J. Drug Dev. & Res., Jul-Sep 2011, 3 (3): 70-84.

6) S. Lakshmi Savithri*, B.Geethika Reddy, K.Sushanth Sekhar, G.Durga, Y.Srilekha, P.Ratnakumari; Review on transdermal drug delivery system; Int J. Pharm. Drug. Anal, Vol: 9, Issue: 4, 2021; 236-240.

7) 1Chanchal Tiwari, 1Mahima Choudhary, 1Princy Malik, 1Pankaj Kumar Jaiswal, 2Reetu Chauhan; Transdermal Patch: A Novel Approach for Transdermal Drug Delivery; Journal of Drug Delivery & Therapeutics. 2022; 12(6):179-188.

8) Anjali V Patel, Biren N Shah; TRANSDERMAL DRUG DELIVERY SYSTEM: A REVIEW;Pharma Science Monitor 9 (1), 2018.

9) Himanshi Tanwar, Ruchika Sachdeva; Transdermal drug delivery system: A review; International journal of pharmaceutical sciences and research 7 (6), 2274, 2016.

10) Eseldin Keleb, Rakesh Kumar Sharma, Esmaeil B Mosa, Abd-Alkadar Z Aljahwi; Transdermal drug delivery system-design and evaluation; International journal of advances in pharmaceutical sciences 1 (3), 2010.

11) Vaibhav Rastogi, Pragya Yadav; Transdermal drug delivery system: An overvie; Asian Journal of Pharmaceutics (AJP) 6 (3), 2012.

12) Audumbar Digambar Mali; An updated review on transdermal drug delivery systems; skin 8 (9), 2015.

13) D Prabhakar, J Sreekanth, KN Jayav; Transdermal drug delivery patches: A review; Journal of Drug Delivery and Therapeutics 3 (4), 231-221, 2013.

14) Das A, Ghosh S, Dey BK, Das S, A novel technique for treating the type-ll diabetes by transdermal patches prepared by using multiple polymer complexes, Int J Pharm Res. Dev, 2010,2(9),195 – 204.

15) Sajid Ali, Maryam Shabbir, Nabeel Shahid; The structure of skin and transdermal drug delivery system-a review; Research journal of pharmacy and technology 8 (2), 103-109, 2015.

16) David Bird, Nuggehalli M Ravindra; Transdermal drug delivery and patches—An overview; Medical Devices & Sensors 3 (6), e10069, 2020.

17) Chetan Ghulaxe, Rameshwar Verma; A review on transdermal drug delivery system; The Pharma Innovation 4 (1, Part A), 37, 2015.

18) Subham Banerjee, Pronobesh Chattopadhyay, Animesh Ghosh, Pinaki Datta, Vijay Veer; Aspect of adhesives in transdermal drug delivery systems; International Journal of Adhesion and Adhesives 50, 70-84, 2014.

19) Gaurav Upadhyay, Shubham Verma, Nayyar Parvez, Pramod Kumar Sharma; Recent trends in transdermal drug delivery system-a review; Advances in biological research 8 (3), 131-138, 2014.

20) Richard H Guy; Transdermal drug delivery; Drug delivery, 399-410, 2010.

21) Ch Nagadev, M Rao, P Venkatesh, D Hepcykalarani, R Prema; A review on transdermal drug delivery systems; Asian Journal of Research in Pharmaceutical Science 10 (2), 109-114, 2020.

22) Ashish Rawat, Ganesh Kumar Bhatt, Preeti Kothiyal; Review on transdermal drug delivery system; Indo Am J Pharm Sci 3, 423-428, 2016.

23) Andrew J Carmichael; Skin sensitivity and transdermal drug delivery: a review of the problem; Drug safety 10 (2), 151-159, 1994.

24) Beverley J Thomas, Barrie C Finni; The transdermal revolution; Drug discovery today 9 (16), 697-703, 2004.

25) Jhawat VC, Saini V, Kamboj S, Maggon N, "Transdermal drug delivery systems: approaches and advancements in drug absorption through the skin" Int J Pharm Sci Rev Res, 2013; 20(1):47-56.

26) Jain, N.K., In; Advances in Controlled and Novel Drug Delivery, 1st Edn., CBS publishers and distributors, 2002, 428-37.

27) Mutalik S, Udupa N, Formulation development, in vitro and in vivo evaluation of membrane controlled transdermal systems of glibenclamide, J Pharm Pharmaceut Sci, 2005, 8, 26-38.

28) Shah VP, Tymes NW and Skelly JP, In vitro release profile of clonidine transdermal therapeutic systems and scopolamine patches, Pharm Res 6:346-351 (1989).