International Journal of Scientific Research in Science, Engineering and Technology
Print ISSN: 2395-1990 | Online ISSN : 2394-4099 (www.ijsrset.com)
doi : https://doi.org/10.32628/IJSRSET23103176

Recent Updates and Advancement of Transdermal Drug Delivery System

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ARTICLEINFO

Article History:

Accepted: 10 June 2023
Published: 24 June 2023

Publication Issue
Volume 10, Issue 3
May-June-2023

Page Number
634-642

ABSTRACT

Tranderrmal drug delivery system is topically used drug administration's which are mainly used in the form patch and the transdermal patch are applied on the skin. TDDS have better drug absorption, good bioavailability and the drug delivered through the skin in a systemic circulation by controlled drug delivery system. Today about 74% of drug are taken orally and that are less side effect, the drug are transported through the viable epidermis to dermis tissue of skin for the local therapeutic effect into the systemic circulation, TDDS avoids the first- pass metabolism , increased therapeutic effect and maintained the plasma drug level. In pharmaceutical industries have many new advancement of technology which modified all resources in TDDS, the drug used as a controlled drug delivery system but now days we used novel drug delivery system which is painless method of drug administration . The scientific development of transdermal patches were comes in 1970s and the first patches were approved in 1979 by FDA for the treatment of motion sickness. Now days, there are many numbers of patches exist in market such as fentanyl, nicotine, clonidine, nitroglycerine, oxybutinin, testosterone, lidnocaine and scopolamine. Along with, the transdermal drug delivery system (TDDS) represents many approaches. In this overview, we describe the different types of TDDS methods available and critically discuss their specific strengths and weaknesses, characterization methods, and the potential of each method. Advances in research on these alternative methods have demonstrated the high performance inherent in the TDDS, which are expected to find application in a wide range of applied.

Keywords :- transdermal drug delivery system, good bioavailability, advance technology, patches, painless drug, systemic circulation, penetration enhancer.

I. INTRODUCTION

A drug delivery system (DDS) is a collection of physicochemical techniques that control how pharmacologically active compounds are transported and released into cells, tissues, and organs, enabling the active chemicals to exert their effects as efficiently as possible [1]. In order to maximize therapeutic efficacy and avoid side effects, DDS addresses the drug delivery methods and formulations that efficiently dispense the medication. Depending on the route of delivery, there are numerous distinct administration techniques, such as oral administration, transdermal administration, lung inhalation, mucosal administration, and intravenous injection. Due to improvements in medication permeation through the stratum corneum and greater bioavailability, therapies can now be delivered directly to the site of action via topical and transdermal drug delivery methods [2].

Recent data on skin illness indicate that necrotizing fasciitis, often known as dermatitis, is the fourth most common cause of nonfatal disease (Seth et al., 2017; Flohr and Hay, 2021). Acne was the second most common skin ailment, according to certain research and 19,726 publications between 2015 and 2020. The table below lists the global burden of skin diseases [3].

Skin diseases	Global burden of skin disease rank	Rank by % of total publications	% Global burden of disease (measured in disability-adjusted life year	Publications between 2015–2020 (N = 19,272), n (%)d
Dermatitis	1	3	0.38	1927
Acne	2	4	0.29	477(2.42)
Psoriasis	3	2	0.19	1936(9.81)
Urticaria	4	7	0.19	139(0.70)
All other skin and subcutaneous diseases	NA	NA	0..12	NA

TABLE 1:- Global burden of skin disease rankings and literature representation between 2015 and 2020

The skin of an adult is approximately 1/3 perfused and covers an area of about 2 m2 [4].

The skin epidermis comprises five anatomical layers. The outermost layer of the epidermis is the stratum corneum [5]. For the administration of various dermatological drugs, skin is the best organ for drug delivery. Drug administration through the skin has been used for the limited pharmacological effect in the tissues of the skin. A stable medication diffuses passively into the interfollicular region of the skin through the intact stratum corneum [6] with neutral molecules. Before being discharged into the systemic circulation, the drug molecules disperse to a target organ to influence the associated tissue and provide a therapeutic effect. Neomycin for superficial infections, benzoyl peroxide for acne, and hydrocortisone for dermatitis are a few examples of dermatology applications.[7].figure no.1:-

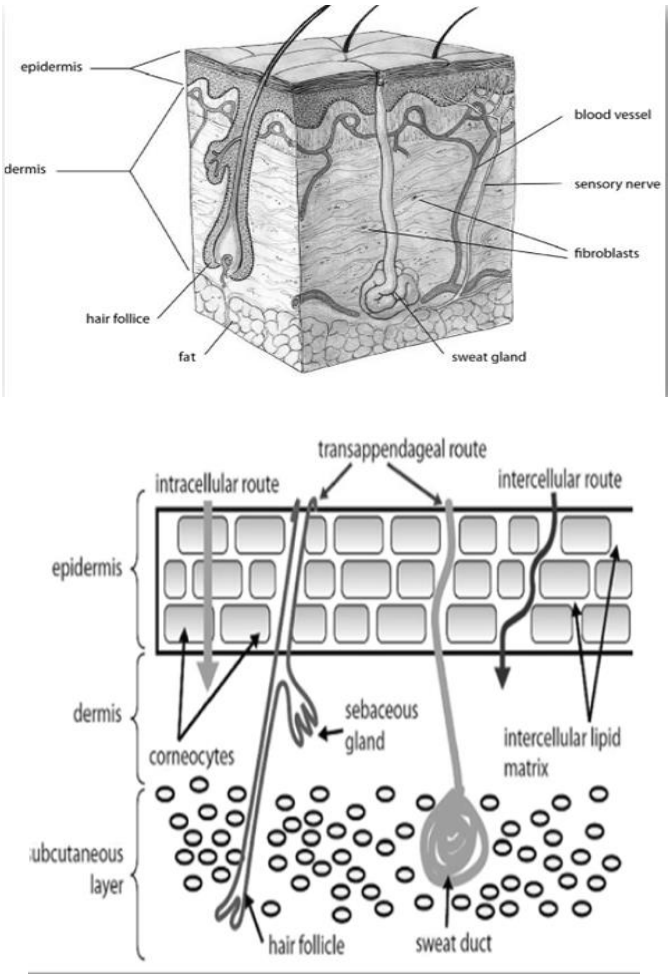

Figure 1:- Schematic diagram of anatomy of skin

A BRIEF HISTROY OF TDDS:-

Transdermal drug delivery is not a new concept, because in 20th century drug was prepared by homemade (herbal) methods for example mustered plaster were used for the chest congestion and belladonna plaster used for the transdermal analgesic, its contain 0.25% of belladonna alkaloid i.e. mentioned on US pharmacopoeia[8]. The 1st generation of TDD is responsible for most of the transdermal patches that have thus far been in clinical use [9]. By consistently reducing a smoker's desire for cigarettes more than 30 years ago, the nicotine patch transformed the effort to stop smoking. Catapres® (clonidine) is the first patch that gives hypertension patients who would typically have to take one tablet twice a day a seven-day[10]. This drug is classified by the sustained drug release form that contains seven days delivery of drug for small molecule. A rivastigmine patch i.e Exelon® introduced in 2007,for the dementia patient and their care giver. The both patient take medicine once-a –day, in this patch has a higher safety profile for e.g., Less nausea and vomiting as compared to capsule and oral solution[11] . The second generation of transdermal delivery systems acknowledges the necessity of improving skin permeability in order to broaden the application of transdermal medications [12]. The best enhancer will (i) boost skin permeability by reversibly altering stratum corneum structure (ii) additional propulsion for travel within the skin (iii) prevent damage to deeper, live tissues. This generation's enhancement techniques, like non-avitational ultrasound, iontophoresis, and conventional chemical enhancers, have had difficulty striking the right balance between increasing stratum corneum delivery and safeguarding deeper tissues from harm[13]. This second generation of delivery technologies has thereby improved localized, dermatological, cosmetic, and some systemic small molecule distribution while having minimal effect on the delivery of macromolecules.

TRANSDERMAL DRUG DELIVERY SYSTEM AND PATIENT COMPLIANCES:-

Now days, the drug advancement and technology which are applied on the skin membrane without causing any irritation, transdermal drug delivery system is the best and easiest form of drug delivery into the systemic circulation, the drug ability directly apply to the site of action. The TDDS has one of the widely accepted routes of administration [14]. The skin is used as a site for sustained drug delivery from the TDS to the systemic circulation, usually by applying a drug-containing patch to the skin. It is a non-invasive, convenient and painless method that avoids gastrointestinal toxicity (e.g. peptic ulcer) and preferentially passes through therapeutic metabolism [15]. Currently, the most common form of drug delivery is the oral route. In addition to its many benefits, this pathway has a tendency for

low bioavailability and spikes in blood levels (both high and low) due to hepatic metabolism (first pass), resulting in high and/or high doses. or frequent medications, which can be costly and inconvenient[16]. Drugs administered in this manner should be effective at daily doses of a few mg per day. The half-life (t1/2) of the drug should be short. The drug should not cause an allergic reaction. Drugs that are degraded in the gastrointestinal tract or inactivated by first-pass effects in the liver are good candidates for transdermal delivery. In the treatment of chronic pain and smoking cessation, it is possible to administer in small amounts by removing the first pass effect. It is also beneficial for patients with reduced liver function, so these patients have fewer side effects. Transdermal patches are less expensive than other formulations because they allow drug delivery from 1 to 7 days. High patient compliance is responsible for market growth.
Although TDS was introduced to the US market in the late 1970s, transdermal administration has been around for a long time [17]

Ideal properties of drug substance for the use of transdermal drug delivery system:-

Parameter	Properties
Dose	Less than 20mg/day
Molecular weight	<400 Dalton
Half life	<10 hrs
Partition coefficient	1 to 4
Melting point	<200°C
ph of the aqueous solution	5-9
Oral bioavailability	Low

RECENT TECHNIQUES USED IN TDDS:-

1. **Iontophoresis**:-This is a process that increases the penetration of topical treatments. The principle of iontophoresis is based on the fact that like charges repel each other and opposite charges attract each others. Thus, when a positively charged drug is delivered during iontophoresis, the charged drug dissolves in the electrolyte surrounding the electrode of similar polarity, i.e. the anode. When an electromotive force is applied, the drug is repelled and travels through the stratum corneum to a cathode located elsewhere in the body[18]
2. **Electroporation**:- This method applies high-voltage electrical pulses ranging from 5 to 500 V for short exposure times (˜ms) to the skin to form tiny pores in the stratum corneum to improve permeability. Drug Diffusion Acceleration. Electrical stimulation is administered using closely spaced electrodes for safe and painless administration of drugs[19].
3. **Sonophoresis**:- Sonophoresis causes destruction of the stratum corneum due to the formation of cavities, micro-occlusions and thermal sensitization[20]. This involves breaking down lipids present in the stratum corneum, allowing drugs to cross the biological barrier.
4. **Microneedles Iontophoresis**: The microneedle drug delivery system is a novel drug delivery system that delivers drugs into the bloodstream through a needle. The drug contains a system in which micron-sized needles pierce the superficial layers of the skin and the drug is diffused through the epidermal layers [21].
5. **TDDS using chemical enhancers (passive delivery)**:-To achieve enhanced transdermal delivery and therapeutic efficacy, drugs should have a low molecular weight (less than 1 kDa), affinity for the lipophilic and hydrophilic phases, short half-life and no skin irritation. The many factors that affect drug penetration through the skin include species, skin age and location, skin temperature, skin condition, site of application, duration of exposure, skin moisture content, pretreatment method, and physical properties of the drug[22].Recent research has focused on aspects of transdermal drug delivery technology, ranging

from the development of chemical enhancers that increase the diffusion of drugs through the skin[22].

RECENT ADVANCEMENT IN TRANSDRMAL DRUG DELIVERY SYSTEM:-

TDDS is the most advance research topic in recent year. The area is in the early stages of development and has a very high publicity scale. Similar trends are observed not only in research groups but also in global market trends. Since 2012, it is an innovative wearable transdermal drug delivery system powered by multiple trigger inputs in the form of stretch, electricity, current, and voltage, visible light, near infrared light, edema, and enzymatic action.

- Mishra et al. (2022), prepared and evaluated the transdermal patches of Simvastatin. By solvent Casting method was utilized by authors for formulating patches. Eudragit grade viz. (RS100 and RL100) were explored for forming patches in proportion (4:6 and 2:8). DBP was utilized as plasticizer and DMSO was employed as penetration enhancer [23].
- Shivalingam *et al.* (2021), fabricated transdermal patches of Pantoprazole.Solvent casting technique was employed as manufacturing technique. PVP K30 and Eudragit L100 along with HPMC E5 were explored as potential film forming polymers. Prepared patches were tested for folding endurance, thickness, content uniformity, weight uniformity, percent uptake moisture, tensile strength, surface pH, in vitro drug release profile and swelling index. It was concluded that patches with composition Eudragit L100: HPMC E5 (1:1) provided best results [24].
- Malvey *et al.* (2021) fabricated Ketorolac tromethamine transdermal patches. HPMC E5 was used as film forming polymers. (PEG 400) was employed for the role of plasticizer. DMSO was the permeation enhancer in the formulation. Solvent casting method was used to prepare patches. The fabricated optimized patches were evaluated for various characteristic properties like drug content, thickness, folding endurance, tensile strength and in vitro dissolution. Patches with HPMC E15 and drug in quantity (200 mg) each with 8 % DMSO was found to be optimized formulation [25].
- Morise *et al.* (2019), prepared and characterized "Transdermal" patches of Scopolamine. Drug was incorporated directly into natural rubber latex membrane. Various evaluation parameters employed were wet ability, SEM, FTIR and assays for hemolysis. Results confirmed that there was no drug- membrane interaction. No hemolysis was seen and other tests also proved that this system could be a good drug delivery option in case of scopolamine [26].
- Wang *et al.* (2015), prepared and evaluated "Transdermal" patches using aceclofenac. Span-20 and limonene were used as penetration enhancers. "Solvent casting method was used for preparation." "Transdermal" patches shown high drug content in range 94.9 to 98.2. Flat surface was obtained with good folding endurance i.e. (120-182). Enhanced drug release (61.02 to 93.4 %) was obtained. "Transdermal" patches had no irritant effect on skin on wistar rats. It was concluded from study that d-limonene provided greater permeation rate of drug as compared to Span 20[27].

METHOD OF PREPARATION OF TRANSDERMAL PATCH:-

Transdermal patch was prepared by the casting method. Firstly, polymer was taken with a minimum quantity (PVP/ HPMC/ CHITOSAN) and taken in a beaker. then the other polymer was also added into the solvent (like PVA) and mixed with magnetic stirrer continuously in clockwise direction ,the plasticizers was added and consistensily mixed and the drug was also mixed with the solvent. Pour the solvent into the Petri disk and wrap with the butter paper and kept on the desiccators glass for 20hrs .stored in closed

container and keep away from the light and cool places [28].

Formulation of transdermal drug delivery system:-

Different types of drug properties should be checked before the selection of the drug. The molecular weight of the drug substance should be less than 1000 Daltons. For the penetration of the drug through the skin it should have an affinity for both lipophilic and hydrophilic phase. The drug which is having a low melting point is a suitable candidate for TDDS. Drug dose should not be more than 50 mg/day. Molecules for the TDDS should be potent. The drug should be stable when it comes into contact with skin. The drug should not be irritant or allergic to the skin. A short biological half-life of the drug molecule is required. The drug should not follow a zero-order kinetic profile for transdermal drug delivery. The ideal dose of transdermal drug delivery is 10 mg/day [29-30].

PHYSIOCHEMICAAL EVALUATION OF TRANSDERMAL:-

TDDS PATCH EVALUATION [31-32]:-

- **Uniformity of weight**:-3 different patches from the individual batch were weighed average and weight was calculated.
- **Thickness of the patch:**-it was measured by the vernier calipers at different points and average value was calculated.
- **Moisture content**:-it was calculated by 3 patches from different batch and value was calculated.
- **Folding endurance:**-this was determined by repeatedly folding one film again and again till the broken.
- **Drug content determination**:-It was determined by cutting patch of size 1cm^2 diameter and dissolving it in Phosphate buffer of pH.

FACTORS AFFECTING TRANSDERMAL PERMEABILITY [33,34,35]:-

The factors that affect the permeability of the skin are classified into following three categories:

Physicochemical properties of the penetrant molecule:-

a) **Partition co-efficient**: water and lipid soluble drug that is well absorbed into the skin. Coefficient of percutaneous permiabiity exhibits a linear dependence on the coefficient of distribution. Changing a carrier can also change the lipid/water partition coefficient of the drug molecules. The partition coefficient of drug molecules can be altered by chemical modification without affecting the drugs pharmacology activity.

b) **Ph condition**:- pH mainly affects the rate of absorption of acidic and basic drugs, and the drug's unchanged form has better penetration. The movement of ionizable particles in aqueous solutions is highly dependent on pH.

c) **Drug concentration**:-Transdermal permeability through mammalian skin is a passive diffusion process and depends on the concentration of penetrating molecules in the superficial layer of the skin

Physicochemical properties of the drug delivery system:-

a) The affinity of the vehicle for the drug molecules: This can affect the release of drug molecules from the carrier. The solubility of the carrier determines the release rate of the drug. The drug release mechanism depends on whether the drug is dissolved or suspended in the delivery system/carrier and the interfacial distribution coefficient of the drug from the delivery system to the skin tissue.

b) Composition of drug delivery:-the composition of the drug delivery system can affect not only the

rate of drug release but also the permeability of SCs due to hydration.

c) Enhancement of transdermal permeation:-Due to the dead nature of SC, the release of drug from the dosage form is low. Therefore, penetration enhancer can cause physiological changes in the SC and enhance the penetration of drugs through the skin.

Physiological and pathological conditions of the skin:-

a) Skin age:-Fetal and infant skin is more permeable than mature adult skin, so percutaneous absorption of topical steroids in children is faster than in adults, whereas water permeability is the same in adults and children.

b) Lipid film:-the secretion of sebaceous gland form a thin lipid film on the surface of the skin, and sebum containing emulsifiers and cellular lipid such as epidermal cells can form a protective film that prevents natural moisturizing factors from being removed. Helps maintain skin barrier function.

c) Skin hydration and skin temperature:-Hydration of SC can increase transdermal permeability. A study of salicylic acid's permeation rate through skin with dry and moist corneas showed that the permeation rate of the most water-soluble ester increased more than the other esters when the tissue was wet. An increase in skin temperature may also increase transdermal absorption by increasing vasodilatation of blood vessels in contact with the skin.

Conclusion and future perspective:-

Transdermal drug delivery systems are currently experiencing tremendous growth in the pharmaceutical field. In many ways, it has proven to be an alternative route for drug delivery that cannot be achieved with other delivery systems. However, the favorable outcome of TDDS is highly dependent on the physiochemical properties of the drug (molecular weight, log P, coefficient of skin permeation, etc.) and strategies to change skin properties (passive or active methods).

II. REFERENCES

[1]. Ahmed A, Karki N, Charde R, Charde M, Ganghare B. Transdermal Drug Delivery System an Overview. Int J Biomed Adv Res. 2011; 2: 38-56.

[2]. Patel A, Visht S, Sharma PK. Transdermal Drug Delivery System: Next Generation Patches. J Drug Discov Dev. 1: 43-65.

[3]. Kumar P, sankar C, mishra B. delivery of macromolecules through skin the Indian pharmacist 2004, 5(3):7-17.

[4]. Kumar R, Philip A. Modified Transdermal Technologies: Breaking the Barriers of Drug Permeation via the Skin. Trop J Pharm Res. 2007, 6(1):633-644.

[5]. Wilson R, Waugh A, grant A (2001) anatomy and physilology in health and illness.(9th Edn) 200001:363-6.

[6]. Tortara GS, grabowski SK (2000) principle of anatomy and physiology,(9th Edn) 140-94.

[7]. Farzaneh Sabbagh, Beom Soo Kim Journal of Controlled Release. 2022, 341:132-146.

[8]. Aarti N, Louk Armp, Russsel Op. Richard Hg. Mechanism of Oleic Acid Induced Skin Permeation Enhancement in Vivo in Humans. Jour. Control. Release. 1995; 37:299-306.

[9]. Baichwal Mr. Polymer Films as Drug Delivery Systems Advances in Drug Delivery Systems. Bombay, Msr Foundation; 1985; 136-147.

[10]. Vyas Sp, Khar Rk. Targetted and Controlled Drug Delivery Novel Carrier System. 1st Ed. Cbs Publishers and Distributors New Delhi. 2002; 411-447.

[11]. Singh J, Tripathi Kt, Sakia Tr. Effect of Penetration Enhancers on The in vitro Transport

of Ephedrine Through Rate Skin and Human Epidermis From Matrix Based Transdermal Formulations. Drug Dev Ind Pharm. 1993; 19:1623-1628.

[12].Michael N Pastore, Yogeshvar N kalia, Michael Horsmann, Michael S Robert review on transdermal, history, development and pharmacology. Bristish journ.of pharmacology 2015;172:2179-2209.

[13]. Mujoriya R, Dhamande KA. Review on transdermal drug delivery system. Res J Sci Tech. 2011;3(4):227–31.

[14].Jain NK, Controlled and novel drug delivery. 1st, CBS Publisher and Distributors, New Delhi. 2001:100- 129.

[15].Dipen patel, sunita A chaudhary, bhavesh parmar, et al. transdermal drug delivery system: a review. 2012;1(4):9.

[16].Rizwan M, Aqil M, Talegoankar S, Azeem A, Sultana Y, Ali A. Enhanced transdermal drug delivery techniques: an extensive review on patents. Recent Pat Drug Delivery & formululation. 2009, 3(2):105-24.

[17].Keith AD, Polymer matrix consideration for Transdermal Devices. Drug DevInd Pharm. 1983, 9: 605-625.

[18].Charoo NA, Rahman Z, Repka MA, Murthy SN. Electroporation: An avenue

[19].for transdermal drug delivery. Curr Drug Deliv. 2010;7(2):125–36. https://doi.org/10.2174/156720110791011765).

[20].Park J, Lee H, Lim GS, Kim N, Kim D, Kim YC. Enhanced transdermal drug delivery bysonophoresis and simultaneous application of sonophoresis & iontophoresis. AAPS PharmSciTech. 2019;20(3):96.

[21].Agrawal S, Gandhi SN, Gurgar P, Saraswathy N. Microneedles: An advancement to transdermal drug delivery system approach. J Appl Pharm Sci. 2020;10(3):149–59.

[22].S. K. P. Kumar, D. Bhowmik, B. Chiranjib, And R. M. Chandira, "Transdermal Drug Delivery System-A Novel Drug Delivery System And Its Market Scope And Opportunities," International Journal Of Pharma And Bio Sciences,2010;1(2):1–21.

[23].Merkle HP. Transdermal delivery systems. Methods Find Exp Clin Pharmacology 1989;11:135-53.

[24].Mishra, S. K. et al. Preparation and Characterization of Transdermal Therapeutic System Containing Simvastatin: A Statistical Study. Indian J. Pharm. Educ. Res.2022; 56, 112–120.

[25].Shivalingam, M. R., Balasubramanian, A. & Ramalingam, K. Formulation and evaluation of transdermal patches of pantoprazole sodium. Int. J. Appl. Pharm.2021; 13, 287–291.

[26].Malvey, S., Rao, V. & Muthu, K. Development and In Vitro Characterisation of Transdermal Therapeutic System of Ketorolac Tromethamine. Orig. Res. Artic. J Evol. Med Dent Sci 2021;10:93–97.

[27].Morise, B. T. et al. Scopolamine loaded in natural rubber latex as a future transdermal patch for sialorrhea treatment. Int. J. Polym. Mater. Polym. Biomater. 2019;68:788–79.

[28].Wang, Y., Zhao, X.-P. & Ruan, J.-W. Transdermal Drug Delivery System of Aceclofenac for Rheumatoid Arthritis and the Effect of Permeation Enhancers: In vitro and in vivo Characterization. Int. J. Pharmacol. 2015;11:456–462.

[29].I.Zurdo Schroeder, P. Franke, U.F. Schaefer, C.-M. Lehr, Development and characterization of film forming polymeric solutions for skin drug delivery, Eur. J. Pharm. Biopharm.2007; 65(1):111-121.

[30].Saxena M, Multalik S, Reddy, MS. Formulation & evaluation of transdermal patches of metoclopramide hydrochloride. Ind Drugs. 2006;43(9):740-5.

[31].Biswajit M, Kanupriya SM, Surajit D, Balaram P. Sorbitan monolaurate 20 as a potential skin

permeation enhancer in transdermal patches, J App Res. 2005;5:96-101.

[32]. Patel RP, Patel G, Patel H, Baria A Formulation and evaluation of transdermal patch of aceclofenac. Res J Pharm Dos Forms Technol. 2009;1(2):108–15.

[33]. Parivesh S, Sumeet D, Abhishek D. Design, evaluation, parameters and marketed products of transdermal patches: A review. J Pharm Res. 2010;3(2):235–40.

[34]. Wang Y, zeng L, song W, Liu J. influencing factors and drug application of iontophoresis in transdermal drug delivery; an overview of recent progress. Drug deliv transl res 2022;12:15-26.

[35]. Charoo NA, Rahman Z, Repka MA, Murthy SN. Electroporation: An avenue for transdermal drug delivery. Curr Drug Deliv. 2010;7(2):125–36.

[36]. Park J, Lee H, Lim GS, Kim N, Kim D, Kim YC. Enhanced transdermal drug delivery by sonophoresis and simultaneous application of sonophoresis and iontophoresis. AAPS PharmSciTech. 2019;20(3):96.

Cite this article as :

Dimpy Jaiswal, Dr. Pushpendra Jain., "Recent Updates and Advancement of Transdermal Drug Delivery System", International Journal of Scientific Research in Science, Engineering and Technology (IJSRSET), Online ISSN : 2394-4099, Print ISSN : 2395-1990, Volume 10 Issue 3, pp. 634-642, May-June 2023. Available at doi : https://doi.org/10.32628/IJSRSET23103176
Journal URL : https://ijsrset.com/IJSRSET23103176