IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

An Overview On Advances In Transdermal Drug Delivery System (TDDS) With Special Case Study On Transdermal Patches

Mr. Achyut R. Kandalkar[1], Prof. Yashkumar A. Meshram[2], Mr. Abhishek R. Kale[3], Mr. Abhijit K. Banait[4], Miss. Aditi D. Jamankar[5]

Jagadambha Institute Of Pharmacy & Research, Kalamb, Maharastra 445401, India[1-5]

ABSTRACT

Transdermal drug delivery systems are substantially used for topically applying medicines in the form of patches and transdermal patches to the skin. More drug immersion, excellent bioavailability, and systemic rotation of the medicine through the skin are all advantages of TDDS. Currently, 74 of specifics are taken orally and have smaller adverse goods. They're carried through the skin's dermis and feasible epidermis for original remedial action and into the bloodstream. TDDS avoids first pass metabolism, adding remedial efficacity and maintaining tube medicine situations. The most extensively used dermatological treatment styles in the history were topically administered poultices and ointment. These phrasings are absorbed via the skin if they've systemic adverse goods, as some of them do. The transdermal delivery system encompasses all topically applied medicine phrasings designed to get the active component into the bloodstream. The review delves into the diverse technologies employed in TDDS, including microneedle arrays, iontophoresis, and novel formulation strategies, elucidating their contributions to enhancing drug permeation across the skin barrier. Furthermore, it discusses the importance of evaluation parameters, history and its application.

A special case study on transdermal patches is presented, offering a detailed examination of their design principles, clinical applications, and recent breakthroughs. The case study incorporates examples of successful transdermal patch products, emphasizing their efficacy, patient compliance, and therapeutic benefits.

KEYWORDS:

Transdermal Drug Delivery System, Transdermal Patches, Penetration Enhancer, Stratum Corneum

INTRODUCTION

A drug delivery system (DDS) is a collection of physicochemical ways that control how pharmacologically active composites are transported and released into cells, apkins, and organs, enabling the active chemicals to ply their goods as efficiently as possible. [1] In order to maximize remedial efficacity and avoid side goods, DDS addresses the medicine delivery styles and phrasings that efficiently apportion the drug. Depending on the route of delivery, there are multitudinous distinct administration ways, similar as oral administration, transdermal administration, lung inhalation, mucosal administration, and intravenous injection. Due to advancements in drug saturation through the stratum corneum and lesser bioavailability, curatives can now be delivered directly to the point of action via topical and transdermal medicine delivery styles[2]

Recent data on skin illness indicate that necrotizing fasciitis, frequently known as dermatitis, is the fourth most common cause of nonfatal complaint. Acne was the alternate most common skin disease, according to certain exploration and 19,726 publications between 2015 and 2020. The table below lists the global burden of skin conditions [3]

Table 1: Global burden of skin disease rankings and literature representation between 2015 and 2020[4]

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

The skin of an grown-up is roughly1/3 perfused and covers an area of about 2 m2. [5] For the administration of colorful dermatological medicines, skin is the stylish organ for medicine delivery. medicine administration through the skin has been used for the limited pharmacological effect in the apkins of the skin. A stable drug diffuses passively into the interfollicular region of the skin through the complete stratum corneum[6] with neutral motes. Neomycin for superficial infections, benzoyl peroxide for acne, and hydrocortisone for dermatitis are a many exemplifications of dermatology operations.[7]

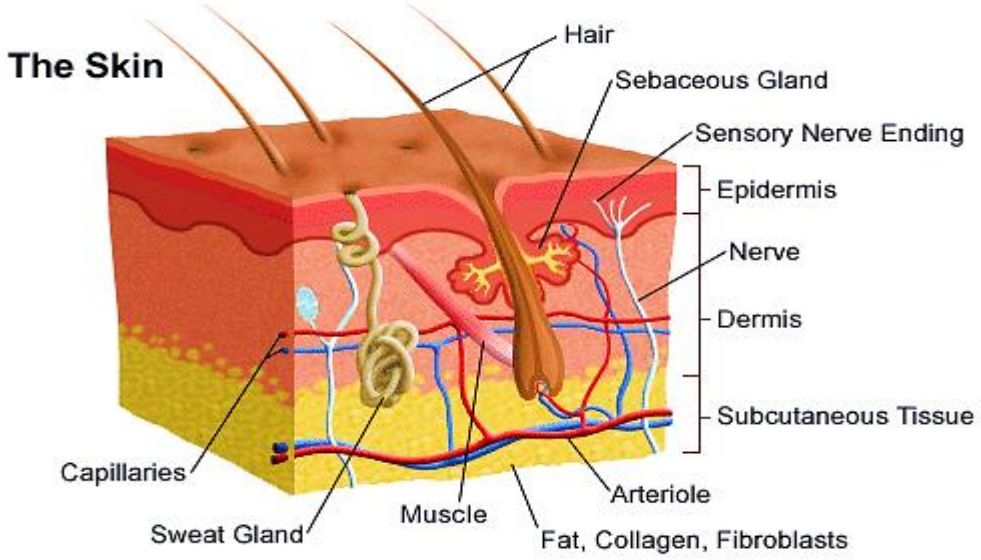

Figure 1: Schematic diagram of anatomy of skin [8]

2. A BRIEF HISTROY OF TDDS

Transdermal medicine delivery isn't a new conception, because in 20th century medicine was prepared by manual(herbal) styles for illustration mustered cataplasm were used for the casket traffic and belladonna cataplasm used for the transdermal analgesic, its contain0.25 of belladonna alkaloid i.e. mentioned on US pharmacopoeia.[9]

First- generation transdermal delivery systems The first generation of transdermal delivery systems is responsible for utmost of the transdermal patches that have therefore far been in clinical use First-generation delivery campaigners must be low- molecular weight, lipophilic and efficient at low boluses. Generally, their transdermal delivery should be more seductive than oral delivery due to low oral bioavailability, the need or desire for lower frequent dosing or steady delivery biographies, or other factors. medicine transport across the stratum corneum generally involves prolixity through the intercellular lipids where hydrophilic motes travel through the lipid head group regions and lipophilic motes travel through the lipidtails.variation on the traditional transdermal patch of first- generation delivery systems involves no patch at each, but applies a metered liquid spray, gel or other topical expression to the skin that, upon evaporation or immersion, can drive small lipophilic medicines into the stratum corneum, which in turn serves as the medicine force for extended release into the feasible epidermis over hours. For illustration, testosterone gels have been in use for several times and a transdermal spray has been lately approved for estradiol delivery.

Alternate- generation transdermal delivery systems The alternate generation of transdermal delivery systems recognizes that skin permeability improvement is demanded to expand the compass of transdermal medicine.. The ideal enhancer should (i) increase skin permeability by reversibly dismembering stratum corneum structure,(ii) give an added driving force for transport into the skin and(iii) avoid injury to deeper, living apkins. still, improvement styles developed in this generation, similar as conventional chemical enhancers, iontophoresis and noncavitational ultrasound, have plodded with the balance between achieving increased delivery across stratum corneum, while guarding deeper apkins from damage. As a result, this alternate generation of delivery systems has advanced clinical practice primarily by perfecting small patch delivery for localized, dermatological, ornamental and some systemic operations, but has made little clinically important effect on the delivery of macromolecule.[10-14]

3. TRANSDERMAL DRUG DELIVERY SYSTEM AND PATIENT COMPLIANCES

Due to advancement in technology and the capability to apply the medicine to the point of action without causing vexation to the skin membrane, Transdermal route is getting a extensively accepted route of medicine administration. Skin is used as point for nonstop medicine administration into the systemic rotation in TDS and generally a patch containing medicine substance is presses on to the skin. It's non invasive, accessible and effortless, and avoids gastrointestinal toxin(e.g. peptic ulcer complaint) and the remedial first pass metabolism. As patient compliance is veritably high in case of TDS so it's getting an instigative and grueling area. Keeping in mind the many advantages that are bandied below we can fluently justify its significance. a. It avoids the pitfalls and nuisances of parenteral remedy. Avoid First pass effect. Reduces diurnal dosing, therefore, perfecting patient compliance. Extends the exertion of medicines having short tube half- life through the force of medicine present in the remedial delivery system and its controlled release characteristics.

Rapid termination of medicine effect by junking of medicine operation from the face of the skin. Enhance remedial efficacy, reduced side goods due to optimization of the blood attention time profile and elimination of palpitation entry of medicines into the systemic rotation. Medicines given by a diurnal cure of the order of a many mg/ day. The partial life(t1/ 2) of the medicine should be short. Transdermal delivery system is getting covetable due to large number of advantages in comparison to other route of medicine administration. As there's no need of frequent dosing administration, this factor makes it more enticing especially in long term treatment. In case of habitual pain treatment and smoking conclusion remedy it allows small amounts to be administered due to elimination of first pass effect. It's also salutary for those cases who have compromised liver and hence lower side goods in similar cases.

As transdermal patches can be used to deliver the medicine from 1 to 7 days so these are affordable in comparison to other lozenge forms. High case compliance is responsible for its adding request. TDS were introduced on to the US request in late 1970’s but transdermal delivery have been in use over a long period of time. But due to advancement in technology a large number of chemical enhancers and also different ways like iontophoresis and ultrasound have been developed for those medicines that can not suffer

unresisting prolixity. Substantially medicines of alternate generation which faces interruption of skin external subcase use fresh driving force for delivery of medicine. It's also helpful for cancer case adding the permeability of skin allows nanoparticles to access and target cancer cells also delivery of lidocaine(a charged patch), for which an iontophoretic delivery system was developed has been done by this route successfully. [15]

4. RECENT TECHNIQUES USED IN TDDS

4.1 Iontophoresis:

Iontophoresis promotes the movement of ions across the membrane under the influence of a small externally applied implicit difference (lower than0.5 mama / cm2), which has been proven to enhance skin penetration and increase release rate of several medicines with poor immersion/ saturation biographies. This fashion has been employed in the in vivo transport of ionic or nonionic medicines by the operation of an electrochemical implicit grade. The efficacy of iontophoresis depends on the opposition, valency, and mobility of the medicine patch, the nature of the applied electrical cycle, and the expression containing the medicine. In particular, the dependence on current makes medicine immersion through iontophoresis less dependent on natural parameters, unlike utmost other medicine delivery systems.

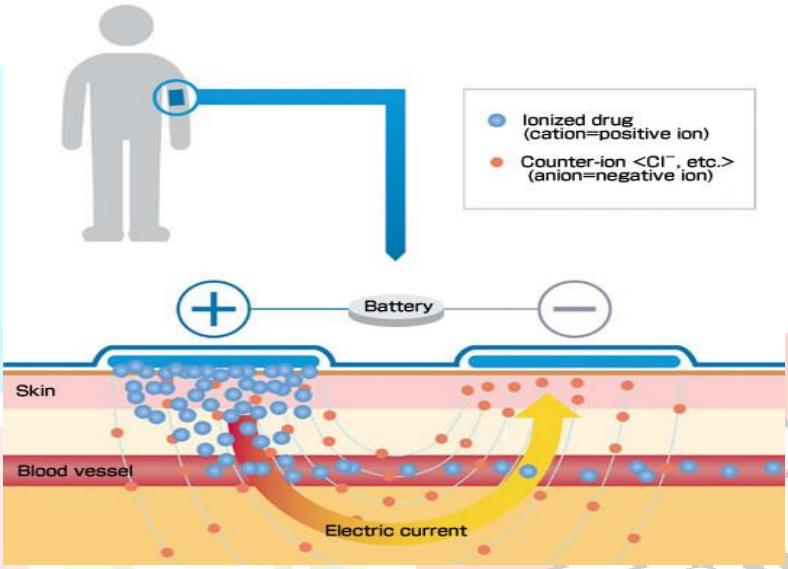

Figure 2: The principle of operation of the patch of iontophoresis [16]

4.2 Sonophoresis:

The desired range of ultrasound frequencies generated by ultrasound device can improve TDDS. Low-frequency ultrasound is more effective, because it facilitates drug movement by an aqueous path in the perturbed bilayer through cavitation. The drug such as a gel or a cream, which transmits ultrasonic waves to the skin and disturb the skin layers, thereby creating an aqueous path through which the drug can be injected. Ultrasound also increases the local temperature of the skin area and creates thermal effect, which further promotes drug penetration. .Several drugs of different classes have been delivered by this method solubility, dissociation and ionization constants, and electrical properties such as mannitol and drugs such as insulin.

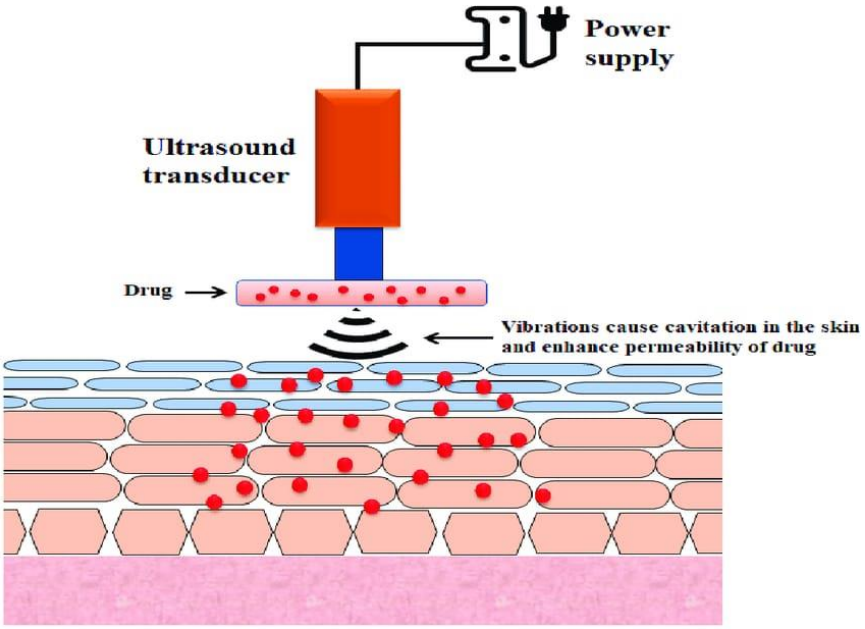

Figure 3: Illustration of Sonophoresis [17]

4.3 Electroporation:

This system uses the operation of high voltage electricpulses ranging from 5 to 500 V for short exposure times (ms) to the skin, which leads to the conformation of small pores in the SC that ameliorate permeability and aid medicine prolixity. For safe and effortlessmedicine administration, electric beats are introduced only low MW medicines, similar as doxorubicin, mannitol, orcalcein, but also high MW bone similar as antiangiogenic peptides, oligonucleotides, etc

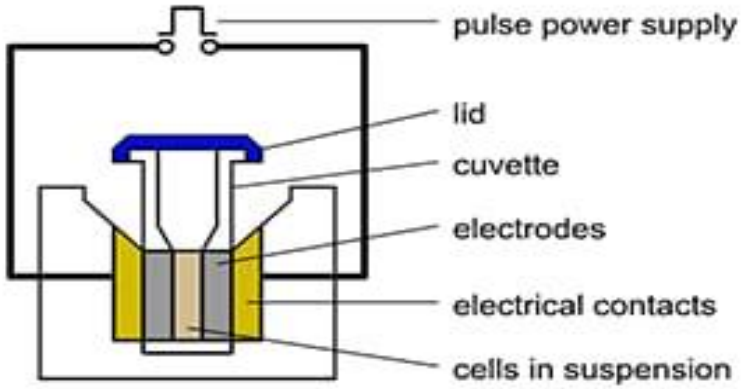

Figure 4: Methods of electroporation [18]

4.4 Microneedle:

The microneedle medicine delivery system is a new medicine delivery system, in which medicines are delivered to the circulatory system through a needle. This involves a system in which micron sized needles pierce the superficial subcaste of the skin, performing in medicine prolixity across the epidermal subcaste.

Because these microneedles are short and thin, these deliver to drug directly to the blood capillary area for active immersion, which helps in avoiding pain Insertion of microneedles into mortal skin, which also represents the broad ideal of exploration on microneedles.[20]

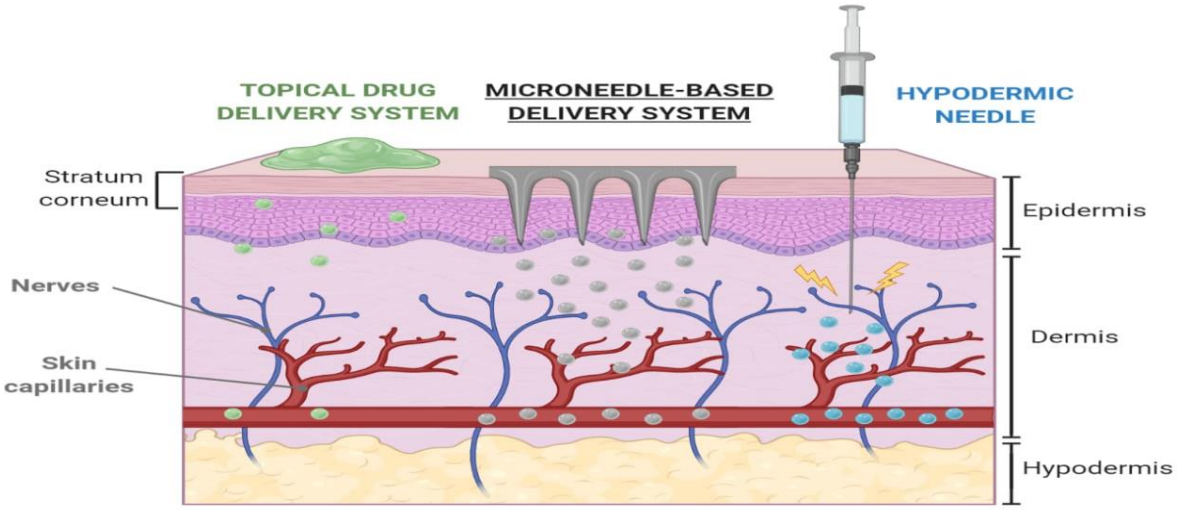

Figure 5: The microneedle medicine delivery system [19]

4.5 TDDS using chemical enhancer:

To achieve enhanced transdermal Delivery and remedialefficacity, medicines should Have a low molecular weight (lower than 1 kda), Affinity for the lipophilic and hydrophilic phases, Short half- life and no skin vexation. The numerous Factors that affect medicine penetration through the Skin include species, skin age and position, skin Temperature, skin condition, point of operation, Duration of exposure, skin humidity content, Pretreatment system, and physical parcels of the medicine recent exploration has concentrated on aspects Of transdermal medicine delivery technology, ranging from the development of chemical enhancers that increase the prolixity of medicines through the skin. [21]

5. ADVANTAGES AND DISADVANTAGES OF TDDS

5.1 Advantages:

- Avoid first- pass metabolism. Transdermal drug offers a nonstop saturation of a substance over a long period of time.
- Patient compliance is increased.
- Adverse events are reduced Intra &inter-patient variability is reduced as a result of the docked drug authority
- No hindrance with the liquids in the bowel and stomach.
- Maintains blood situations that are stable, constant, and under control for a longer period of time. [22]

5.2 Disadvantages:

- Limited Permeability for Large Molecules:
- Skin Irritation and Allergic Reactions:
- Slow Onset of Action:
- Limited Drug Loading Capacity:
- Patient Variability in Skin Permeability:
- Risk of Systemic Toxicity:
- Formulation Challenges: [23]

6. METHODS OF PREPARATION OF TRANSDERMAL PATCH [24,25]

1. Asymmetric TPX membrane method.
2. Circular Teflon mould method.
3. Mercury substrate method.
4. Through the the utilization of "IPM membrane" technology,
5. By using “EVAC membranes” method.
6. Preparation of TDDS by using proliposomes.
7. By using free film method.

6.1 Asymmetric TPX membrane system:

The backing membrane for a prototype patch will be a heat sealable polyester distance(type 1009, 3m) with a 1 cm fringe concave. The drug sample is allocated into the concave membrane, which is subsequently sealed with an tenacious and covered by an asymmetric TPX poly(4- methyl-1-pentene) membrane. The dry/ wet inversion procedure is used to make them. To make a polymer result, TPX is dissolved in a amalgamation of soap(cyclohexane) and non solvent ingredients at 60 °C. The polymer result is maintained at 40 °C for 24 hours before being cast on a glass plate with a Gardner knife to apre- set viscosity. After that, the casting film is faded at 50 °C for 30 seconds, and the glass plate is directly immersed in the coagulation bath(at 25 °C). The membrane can be removed after 10 beats of immersion and dried in a gyration rotisserie at 50 °C for 12 hours.

6.2 Circular Teflon method:

In an organic detergent, results containing polymers in colorful rates are utilised. The quantum of drug calculated is dissolved in half the quantum of the same organic detergent. Enhancers are dissolved in the other half of the organic detergent and also added in colorful attention. As a plasticizer, di-n-butyl phthalate is added to the medicine polymer result. The entire admixture must be stirred for 12 hours before being placed into aindirect Teflon mould. In a laminar inflow hood model with an air speed of0.5 m/ s, the moulds should be deposited on a levelled face and covered with a reversed channel to manage solvent vaporization. After 24 hours, the detergent is allowed to dematerialize. To exclude geriatric goods, the dried flicks must be held for another 24 hours at250.5 °C in a desiccator containing silica gel before being estimated. Within one week of their medication, the type flicks must be reviewed.

6.3 Through the the utilization of "IPM membrane" technology:

The pharmaceutical substance is combined with a mixture of water and propylene glycol, including carbomer 940 polymers, and agitated for 12 hours using an elegant stirring device. By introducing triethanolamine, the dispersion is neutralized and becomes viscous, while maintaining a pH of 7 in the buffer. In cases where the drug's solubility in an aqueous environment is inadequate, the use of "thirsty result" can be employed to form a gel. This resulting gel will then be seamlessly incorporated into the IPM membrane.

6.4 Preparation of TDDS by using proliposomes:

A film deposit system and a carrier system are used to produce the proliposomes. Lecithin with the rate of0.12.0 can be used as a bettered interpretation of the previous reference medicine. 5 mg of mannitol greasepaint is placed in a 100 ml round bottom beaker that's kept at 60- 70 °C and spun at 80- 90 rpm for 30 twinkles while vacuum drying the mannitol. After drying, the water bath's temperature is set at 20- 30 °C. At 37 °C, a0.5 ml aliquot of the organic result is placed in the round bottomed beaker, and after complete drying, fresh0.5 ml aliquots of the result are added. The medicine- loaded mannitol maquillages (proliposomes) are placed in a desiccator overnight and settled through a 100 fortitude sieve after the final lading. The greasepaint is collected and placed in a glass bottle to be stored at a low temperature until characterization

6.5 By using free film method:

Casting on a mercury face produces a free cellulose acetate film. Chloroform is used to make a 2 percent w/ w polymer result. Plasticizers are used at a 40 percent weight- to- weight rate in the polymer. Five ml of polymer result was placed in a glass ring that was placed over the mercury face in a glass petri dish. An reversed channel was placed over the petridish to control the rate of solvent evaporation. Observing the mercury face after the detergent has fully faded reveals the lm creation. The dried lm will be separated and

stored in desiccators between wax paper wastes until demanded. By varying the volume of the polymer result, free flicks of colorful density can be created.

7. EXPRESSION OF TDDS

The quantity of medication that can be accommodated within a transdermal drug delivery system (TDDS) and the quantity that can effectively penetrate the skin may vary. The capacity for drug loading in the device is determined by the specific device and its technology. Meanwhile, the quantity that successfully permeates the skin is influenced by the formulation and the drug itself.

8. RECENT ADVANCEMENT IN TRANSDRMAL DRUG DELIVERY SYSTEM

TDDS is the most advance exploration content in recent time. The area is in the early stages of development and has a veritably high hype scale. Analogous trends are observed not only in exploration groups but also in global request trends. There have been several advances in the field of transdermal medicine delivery. These include the design of new patches, which include the capability to smell and release medicines directly, advanced lading, and enhanced penetration and release of medicines. Overall, the field of transdermal medicine delivery is an active area of exploration and development, with numerous instigative new developments on the horizon, as bandied below.

8.1 Nanotechnology:

Nanotechnology has shown great eventuality in the advancement of topical and transdermal medicine delivery, other arising technologies and approaches have also shown conceivable prospective in bettered medicine delivery. One similar illustration are biologics, which are getting decreasingly popular in transdermal delivery owing to the presence of natural walls limiting medicine saturation. New rectifiers similar asanti-IL-13 asset (tralokinumab), Janus kinase(JAK) impediments(baricitinib, tofacitinib), andanti-IL-4Rα antibody(dupilumab) are presently being delved in the treatment of seditious conditions. The Food and Drug Administration (FDA) has lately approved the first topical JAK asset ruxolitinib cream for the treatment of mild to moderate atopic dermatitis not sufficiently treatable with tradition topical curatives. Hyaluronic- acid- grounded systems are also getting adding popular as they're extensively used in the pharmaceutical assiduity for their enhanced permeability and biocompatibility. Hyaluronic acid is generally incorporated into nanoparticles, ethosomes, and liposomal transdermal systems, in the treatment of anti-inflammatory conditions similar as atopic dermatitis and psoriasis. Physical penetration fashion like Microneddle, Sonophoresis, ionphoresisetc are used to enhance skin permeability, hydrophilic medicine and ferocious clinical studies.

8.2 Patch Technology for protein delivery:

i. Transdermal delivery of large proteins is new and instigative delivery system. There's no marketable technology presently available for that.
ii. Transpharma uses its unique published patch technology, similar patches contains accurate boluses of proteins in dry state.
iii. It's supposed that largely H2O answerable proteins are dissolved by interstitial fluid i.e. buried from skin through RF- micro channels, into the feasible apkins of the skin, diffusing across steep attention grade.[26]

8.3 Pain-free diabetic monitoring using transdermal patches:

It becomes exercising micro-heating rudiments integrated into the structural subcaste of the patch closest to the skin face, high temperature heat palpitation can be applied locally, violating stratum corneum.
ii. During this process, the skin face gests temperature of 1300C for 30 twinkles.
iii. The temperature diminishes fleetly from the skin face and neither living towel nor the whim-whams consummations are affected. This is effortless and bloodless process, the size of hair follicle, allowing the interstitial fluid to interact with the patch's electrode spots [26].

8.4 Dissolving / Degradable Patches:

These patches are designed to dissolve on the skin and don't need to be removed and discarded. In general, these patches are made from biodegradable accoutrements that are absorbed by the body after use. In a evidence- of- conception paper published in 2019, experimenters successfully administered the antibiotic gentamicin via a dissolving patch in a mouse model of bacterial infection. The results showed that a gentamicin- dissolving microarray patch applied to mouse cognizance could control Klebsiella pneumoniae infection. Dissolving patches for insulin delivery achieves a satisfactory relative bioavailability (RBA)

compared to conventional subcutaneous injection, demonstrating the effectiveness of dissolving patches for diabetes treatment [27]

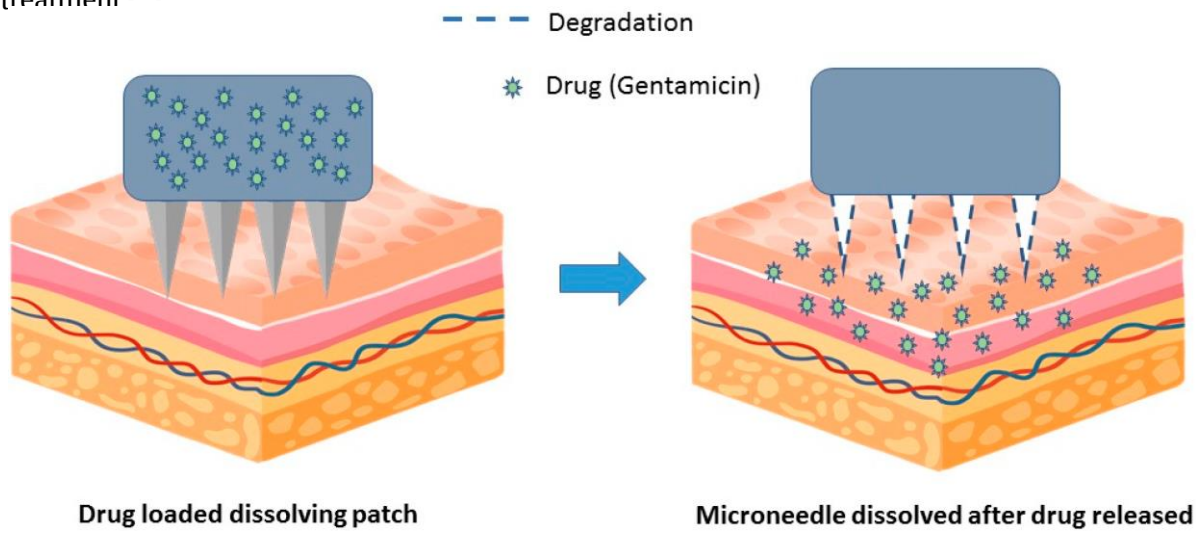

Figure 6: Dissolving/Degradable Patches [28]

8.5 Transdermal Patches For Gene Therapy:

Climate change has likely led to the decline of some of Scotland's mountain shops, according to new research Scientists said numerous of the species reckoned on snow cover remaining high on hills until late spring and indeed summer to insure a wettish environment. They also said shops that thrived on lower ground in warmer conditions were spreading to mountain habitats.Species set up to be in decline include snow pearlwort, alpine lady- fern and alpine speedwell. The exploration by the Botanical Society of Britain and Ireland (BSBI) has taken 20 times to complete and has been published in the new Plant Atlas. Data used to produce the report included further than three million factory records of 2,555 species collected by hundreds of botanists across Scotland. Climate change, niche loss and the spread of non-native species were set up to crucial pitfalls to the health of British and Irish native shops. BSBI said ruinous losses of species in Scotland were among the findings. nearly the entire British population of snow pearlwort is set up on Ben Lawers, but half of the Perthshire mountain's known colonies have faded over the last 40 times.

Fig 7: Transdermal Patches for Gene Therapy & Skin Recovery [29]

9. PHYSIOCHEMICAL EVALUATION OF TDDS

9.1 Consistence:

The consistence of transdermal film is determined by travelling microscope, telephone hand. Screw hand or micrometer at different point of the film.

9.2 Uniformity of medicine:

Weight variation is studied by collectively weighting to aimlessly named patches calculating the average weight. The individual weight shouldn't diverge significantly from the average weight.

9.3 Dug content determination:

Directly counted portion of the film is dissolved in suitable detergent in which medicine is answerable and estimated spectrophotometrically.

9.4 Content uniformity test:

10 patches are named and content in between 85 to 115 of the specified value and bone has content not lower than 75 to 125 of the specified value, also transdermal patches pass the test of content uniformity. But if 3 patches have content in the range of 75 to 125, also fresh 20 patches are tested for medicine content. If these 20 patches have range from 85 to 115 also the transdermal patches pass the test.

9.5 Humidity content:

The set flicks are counted collectively and kept in a desiccators containing calcium chloride at room temperature for 24 hr. [4]

10. FACTORS AFFECTING TRANSDERMAL MEDICINE DELIVERY SYSTEM

The factor affecting skin permeability are as follows [26]

10.1 Biological factors

I. Skin Condition:

The complete skin itself acts as hedge but numerous agents like acids, alkali cross the hedge cells and penetrates through the skin, numerous detergents open the complex thick structure of wanton subcaste detergents like Methanol, Chloroform spread lipid bit, forming artificial shunts through which medicine motes can pass fluently.

II. Skin age:

It's seen that the skin of grown-ups and youthful bones are more passable than aged bones but there's no dramatic difference. Children shows poisonous goods because of the lesser face area per unit body weight. Therefore potent steroids, boric acids, hexachlorophene have produced severe side goods.

III. Blood force:

Changes in supplemental rotation can affect transdermal immersion.

IV. Skin metabolism:

Skin metabolizes steroids, hormones, chemical carcinogens and some medicines. So skin metabolism determines efficacy of medicine percolated through the skin.

10.2 Physicochemical factors:

I. Skin Hydration:

Generally when water saturates the skin, it swells the apkins, soften wrinkles on the skin and its permeability increases for the medicine motes that access through the skin.

II. Partition Measure:

The optimal partition measure(K) is needed for good action. Medicines with high K aren't ready to leave the lipid portion of the skin. Also, medicines with low K won't be percolated The optimal partition measure(

K) is needed for good action. medicines with high K aren't ready to leave the lipid portion of the skin. Also, medicines with low K won't be percolated . The optimal partition measure(K) is needed for .

III. Molecular size and shape:

Medicine immersion is equally related to molecular weight, small motes access briskly faster than large bones.

IV. Temperature and PH of the skin:

The penetration rate varies of if the temperature varies and the prolixity measure decreases as the temperature falls; still acceptable apparel on the body prevents wide oscillations in temperature and penetration rates. According to PH, only unionized motespass readily across the lipid membrane, and week acids and bases disconnect to different degrees according to their pH and pKa or pKb values. Therefore the attention of unionized medicine in applied phase will determine the effective membrane grade, which is directly related to its pH

11. PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS OF THE SKIN: [30]

11.1 Skin age:

Fetal and infant skin is more passable than mature adult skin, so percutaneous immersion of topical steroids in children is faster than in grown-ups, whereas water a permeability is the same in grown-ups and children.

11.2 Lipid film:

The stashing of sebaceous gland form a thin lipid film on the face of the skin, and sebum containing emulsifiers and cellular lipid similar as epidermal ood action. Medicines with high K aren't ready to leave the lipid portion of the skin. Also, medicines with low K won't be percolated cells can form a protective film that prevents natural moisturizing factors from being removed. Helps maintain skin barrier function.

11.3 Skin hydration and skin temperature:

Hydration of SC can increase transdermal permeability. A study of salicylic acid's saturation rate through skin with dry and wettish corneas showed that the saturation rate of the most water-answerable ester increased further than theother esters when the towel was wet. An increase in skin temperature may also increase transdermal immersion by adding vasodilatation of blood vessels in contact with the skin.

12. APPLICATION OF TDDS

Transdermal Drug Delivery Systems (TDDS) find diverse applications across various therapeutic areas. Here are some of the different applications of TDDS along with brief descriptions and references:

12.1 Pain Management:

TDDS is extensively used for the management of chronic pain conditions, offering controlled and sustained release of analgesic drugs.

11.2 Hormone Replacement Therapy:

TDDS is employed in hormone replacement therapy, delivering hormones such as estrogen and testosterone for the treatment of hormonal imbalances.

11.3 Cardiovascular Disorders:

TDDS is utilized for delivering medications for the management of cardiovascular conditions, such as nitroglycerin for angina.

11.4 Smoking Cessation:

TDDS aids in smoking cessation by delivering nicotine through the skin, helping individuals overcome addiction.

11.5 Neurological Disorders:

TDDS is explored for delivering drugs to treat neurological disorders, including medications for Alzheimer's disease and Parkinson's disease.

11.6 Contraception:

TDDS is investigated for delivering contraceptive drugs, providing a non-invasive alternative for birth control.

11.7 Psychiatric Disorders:

TDDS is explored for delivering drugs to manage psychiatric disorders, offering a controlled release for improved patient compliance. [31-33]

12. CASE STUDY IN TRANSDERMAL PATCHES

Transdermal drug delivery devices, commonly referred to as patches, apply medications topically or systemically by using the human skin as a conduit. Scopolamine was the first transdermal patch to be introduced to the market in 1981 as a motion sickness remedy. Since then, advancements have made these systems a lucrative avenue for medication delivery and a significant sector of the pharmaceutical business. The UK Company Medherant Ltd. began by developing novel medicine delivery technology, and their goal is to achieve it.

Compared to more traditional methods like oral consumption and hypodermic injections, transdermal medication delivery has a number of strong advantages. Patients are more likely to adhere to treatment, which is the most evident benefit. Crucially, the medication is administered directly to the site of need, bypassing the liver's first-pass metabolism and the stomach's breakdown, so increasing its bioavailability. Transdermal delivery systems are also widely used since they are non-invasive, self-administered, and often affordable. They provide regulated release of a medicine over an extended period of time.

The most common patch design is the matrix system, which incorporates the drug into the adhesive matrix and distributes it uniformly throughout the patch. The reservoir system regulates drug administration through a rate-controlling membrane. A drug-in-adhesive patch's fundamental parts are the drug, the adhesive matrix, a release liner—which is removed before use—to protect the medication during storage, and a backing that shields the patch from the outside world. Depending on the system being utilized, additional parts, such as penetration enhancers, may be needed.

In 2015, Mercia Technologies Plc, an investment organization that backs life science initiatives from British institutions, provided early finance for Medherant Ltd, a spin-out of Warwick University. Their objective was to create a novel patch that would circumvent the constraints of presently available goods and broaden the range of medications that can be administered transdermally.

The drug-in-adhesive system of the TEPI patch uses a novel polymer pressure-sensitive adhesive technology that was first created by the international adhesives business Bostik. The majority of the over 40 medications that Medherant has identified as potentially suitable for administration via its technology have substantial payloads and are soluble in their free base/acid form. Furthermore, compared to other approaches, less medication is left in the patch after use, allowing the patch to provide a substantial dose over an extended period of time.

Currently, Medherant is working on items from many medication classes, such as hormones, stimulants, and opioids, and is developing a patch that contains ibuprofen for pain management. Additionally, they have created a high-throughput permeation device that allows them to test the formulation features of the active pharmaceutical ingredient fractionally more quickly than they could with a traditional assay. [34]

CONCLUSION

This review explores the evolution of Transdermal Drug Delivery Systems (TDDS), highlighting their significant role in modern healthcare. Innovative technologies like microneedle arrays, iontophoresis, and novel formulations have improved drug delivery efficiency, patient compliance, and therapeutic outcomes. The review emphasizes the need for ongoing research to address skin permeation, formulation stability, and personalized medicine. Interdisciplinary collaboration among scientists, engineers, and medical professionals is crucial for the success of TDDS. The future of TDDS lies in the integration of advanced materials, nanotechnology, and precision medicine approaches, which could revolutionize medical treatment and improve patient well-being.

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. Transdermdelivery system. al 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. Jaiswal, D., & Jain, P. (1927). Recent Updates and Advancement of Transdermal Drug Delivery System. *Dermatitis*, *1*(3), 0-38.
5. 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.
6. Wilson R, Waugh A, grant A (2001) anatomy and physilology in health and illness.(9th Edn) 200001:363-6.
7. Tortara GS, grabowski SK (2000) principle of anatomy and physiology,(9th Edn) 140- 94.
8. Automatic diagnosis of melanoma from dermoscopic images of melanocytic tumors : Analytical and comparative approaches. - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Skin-layers-source-17_fig1_295647033 [accessed 25 Dec, 2023]
9. Farzaneh Sabbagh, BeomSoo Kim Journal of Controlled Release. 2022, 341:132-146.
10. Aarti N, LoukArmp, Russsel Op. Richard Hg. Mechanism of Oleic Acid Induced Skin Permeation Enhancement in Vivo in Humans. Jour. Control. Release. 1995; 37:299-306
11. Guy, R.H. &Hadgraft, J. (eds.) Transdermal Drug Delivery (Marcel Dekker, New York; (2003).
12. Williams, A. Transdermal and Topical Drug Delivery (Pharmaceutical Press, London; 2003).
13. Prausnitz, M.R., Mitragotri, S. & Langer, R. Current status and future potential of trans- dermal drug delivery. Nat. Rev. Drug Discov. 3, 115–124 (2004).
14. Bronaugh, R.L. &Maibach, H.I. (eds.) Percutaneous Absorption, edn. 4 (Marcel Dekker, New York; 2005).
15. Dipen Patel, Sunita A Chaudhary, BhaveshParmar, et al. Trans–dermal drug delivery system: a review. 2012;1(4):9.
16. https://phamix.com/2011/03/08/iontophoresis-a-new-skin-care-technology/
17. Delivery of Insulin via Skin Route for the Management of Diabetes Mellitus: Approaches for Breaching the Obstacles - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Illustration-of-the-basic-design-of-sonophoretic-delivery-devices_fig2_348509956 [accessed 25 Dec, 2023]
18. https://upload.wikimedia.org/wikipedia/commons/7/70/Electroporation_Diagram.png
19. Guillot AJ, Cordeiro AS, Donnelly RF, Montesinos MC, Garrigues TM, Melero A. Microneedle-Based Delivery: An Overview of Current Applications and Trends. *Pharmaceutics*. 2020; 12(6):569. https://doi.org/10.3390/pharmaceutics12060569
20. biomaterialsres.biomedcentral.com/articles/10.1186/s40824-021-00226-6
21. 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.
22. Kajal, D. R. S., Pandit, V., & Ashawat, M. S. (2022). Recent Advancement In Transdermal Drug Delivery System (Tdds). *Journal of Positive School Psychology*, *6*(8), 8882-8892.
23. Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. Nature Biotechnology, 26(11), 1261–1268.
24. Halder, S., Chakraborty, P. ., Pradhan, D. ., & Bagchi, A. (2021). Recent advancement in the method of transdermal drug delivery system: A review. Journal of Applied Pharmaceutical Research, 9(2), 06-09. https://doi.org/10.18231/j.joapr.2021.06.09
25. media.neliti.com/media/publications/432488-recent-advancement-in-the-method-of- tran-e3242a3a.pdf
26. Trupti Mangesh Kumbhakarn et al. Recent Advances in Transdermal Drug Delivery System. Indo American Journal of Pharmaceutical Research.2020:10(09)
27. Wong, W.F.; Ang, K.P.; Sethi,G.; Looi, C.Y. Recent Advancement of Medical Patch for Transdermal DrugDelivery. Medicina 2023, 59, 778 doi.org/10.3390/medicina59040778
28. https://www.mdpi.com/medicina/medicina-59-00778/article_deploy/html/images/medicina-59-00778-g005.png
29. https://link.springer.com/article/10.1007/s13346-022-01138-1/figures/2

30. Cheng T, Tai Z, Shen M, Li Y, Yu J, Wang J, Zhu Q, Chen Z. Advance and Challenges in the Treatment of Skin Diseases with the Transdermal Drug Delivery System. *Pharmaceutics*. 2023; 15(8):2165. https://doi.org/10.3390/pharmaceutics15082165
31. Kalia, Y. N., & Guy, R. H. (Eds.). (2001). Transdermal Drug Delivery: Developmental Issues and Research Initiatives. Marcel Dekker.
32. Murthy, S. N., Wijaya, W., Sinha, V. R., & Bi, J. (2005). Polymeric systems for controlled drug release. In Polymeric Drug Delivery Systems (pp. 1–71). CRC Press.
33. Barry, B. W. (2001). Novel mechanisms and devices to enable successful transdermal drug delivery. European Journal of Pharmaceutical Sciences, 14(2), 101–114
34. A case study in transdermal drug delivery – Medherant https://www.medherant.co.uk/sites/default/files/documents/InventiveStepPatch%20NikolaouHaddleton%20May2018.pdf