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TRANSDERMAL DRUG DELIVERY SYSTEM: ADVANTAGES AND LIMITATIONS

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ABSTRACT

Human civilizations have used chemicals as aesthetic and therapeutic agents on the skin for thousands of years. The use of the skin as a medicine delivery method did not begin until the 20th century, however. In reality, Merriam Webster dates the term "transdermal" to 1944, underscoring the fact that it is a relatively new idea in the field of medicine and pharmaceuticals. Transdermal medications come in distinct, self-contained dose forms. Drug distribution via the skin to have an overall impact without causing changes in the drug's plasma concentration. This review article briefly discusses the benefits of transdermal drug delivery systems (TDDS), skin channels for TDDS, basic clinical concerns in using TDDS, and TDDS limitations. Because of the patches' significant benefits over alternative controlled drug delivery methods, their effectiveness has been shown.

KEYWORDS: Transdermal, Drug delivery, Advantages, Limitation

INTRODUCTION

Transdermal drug delivery systems (TDDS), commonly referred to as "patches," are medication dosage forms intended to disperse a quantity of medication over a patient's skin that is therapeutically effective. The whole morphological, biophysical, and physicochemical features of the skin must be taken into account in order to transport medicinal substances via the human skin for systemic effects. Because it improves patient compliance and avoids first pass metabolism, transdermal administration has an advantage over injectable and oral methods. Transdermal delivery enables for continuous infusion of medications with short biological half-lives, eliminates pulsed entrance into the systemic circulation, which often results in unfavorable side effects, and offers regulated, constant drug administration. This led to the emergence of several novel drug delivery methods, including transdermal, controlled release, and transmucosal. Limiting hepatic first pass metabolism, improving therapeutic effectiveness, and maintaining a constant plasma level of the medication are only a few of the significant benefits of transdermal drug administration. The FDA authorized the first transdermal device, Transderm-SCOP, in 1979 for the treatment of motion sickness and nausea brought on by travel, especially by sea. Measurable blood levels of the medication, detectable excretion of the drug and its metabolites in the urine, and the clinical reaction of the patient to the prescribed pharmacological treatment are all ways to find evidence of percutaneous drug absorption.

The first transdermal patch authorized by the FDA in 1981 was a scopolamine patch. Scopolamine and nitroglycerine are both delivered trans dermally and used to treat a variety of conditions, including angina pectoris associated with coronary artery disease (Transderm Nitro) and motion sickness

(TransdermScop, ALZA Corp.). Patients benefit therapeutically from transdermal medication delivery products. For usage internationally and for sale in the US, more than 35 transdermal medication delivery solutions with around 16 active components each have received approval.

LITERATURE REVIEW

K Purushotham et.al (2023) Transdermal drug delivery systems (TDDS), sometimes known as "patches," are dosage forms that are designed to disperse a therapeutically effective quantity of medication over a patient's skin in order to achieve systemic effects. Transdermal drug delivery systems are used to provide medications that are administered topically. In order to distribute the active ingredient after passing through the skin barriers and prevent first pass metabolism, these pharmaceutical preparations come in a variety of sizes and include one or more active components. They are designed to be applied to the unbroken skin. Approximately 74% of medications administered today are taken orally and are not as effective as expected. Transdermal medication delivery systems were developed to increase effectiveness. The medication quickly reaches the target spot and permeates the skin in TDDS. Transdermal medication delivery devices were created to get past the issues with oral drug administration. Since 1981, these systems have been used for safe and dependable medication administration.

Woo Yeup Jeong et.al (2021) As an alternative to traditional needle injections, a number of non-invasive administrations have lately surfaced. The least unattractive approach among them is a transdermal drug delivery system (TDDS), which has a low rejection rate, good ease of administration, and outstanding patient convenience and persistence. The skin care sector, including cosmetics, as well as the pharmaceutical business may be able to use TDDS. This strategy may avoid local drug concentration builds-up and non-targeted medication delivery since it primarily requires local administration. However, the physicochemical characteristics of the skin result in a number of challenges and limitations for transdermal distribution, and several studies have been done to address these bottlenecks. In this study, we present the many kinds of TDDS approaches that are now available and critically examine the benefits and drawbacks, characterization techniques, and potential of each method. Research on these alternative approaches has advanced, demonstrating the great efficiency of TDDS, which is anticipated to find applications in a variety of industries.

Merugu Rajashekar et.al (2021) By using transdermal patches, users may avoid issues with first-pass viscus metabolism, catalytic digestion attacks, drug reactivity and degradation in acidic conditions, medication fluctuations, and epithelial duct irritation associated with oral drug administration. This paper discusses the many transcutaneous patches available on the market, their kinds, structural components, chemical compound functions, and therefore the necessary evaluation techniques. While there are many medical uses for transdermal patches, including the cessation of smoking, pain treatment, pathology, birth prevention, illness, angina, and internal organ diseases, breakthroughs in formulation research are being made to create transcutaneous patches that can deliver more potent medication. The

design and development of transdermal patches will take into account the chemical scientific qualities of active and inactive components as well as their applicability for long-term usage. Therefore, many chemical methods and physical procedures for the production of skin patches are being investigated.

Maryam Shabbir (2018) The purpose of the current research was to prepare tizanidine HCl transdermal patches, assess the impact of polymers on the drug's in vitro release pattern, and examine the impact of permeation enhancers on the drug's penetration into rabbit skin. Span 20 or DMSO was utilized as a permeation enhancer, and different ratios of hydrophilic (HPMC) and hydrophobic (Eudragit L-100) polymers were combined with PEG 400 as a film-forming agent. Physicochemical properties and in vitro drug release tests were performed on the formulations using the USP paddle over disc technique in phosphate buffered saline (pH 7.4) at 32.0 1°C. S03-A and S04-A were chosen for further ex vivo analysis at Eudragit: HPMC ratios of 8: 2 and 7: 3, respectively, based on in vitro tests and physicochemical assessments. Using a Franz diffusion cell, the effects of various doses of Span 20 and DMSO were examined on excised rabbit skin. Calculated drug flux, permeation, permeability, target flux, and enhancement ratios were compared to control formulations. To assess the drug release patterns, Tukey's multiple comparison test and kinetic models were also used. The biggest improvement in drug permeability was generated by formulation SB03-PE, which combined Span 20 (15% w/w) with Eudragit L-100: HPMC (7:3) and used a zero-order kinetic model with a super case-II drug release mechanism.

ADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEM (TDDS)

The following are some benefits of transdermal distribution over other conventional delivery methods:

1. Bypassing intestinal, salivary, and hepatic first pass metabolism, medicines have increased bioavailability and effectiveness.
2. Self-management is feasible.
3. In an emergency, stopping the patch at any point during treatment by removing the application from the skin's surface is a quick and effective way to halt the active ingredient intake.
4. little difference between and between patients since practically all individuals have essentially the same skin's structure and biochemical makeup.
5. Keeping gastrointestinal incompatibility at bay.
6. Since it is simple to use, it reduces the risks and pain of parenteral medication and increases patient compliance.
7. Optimal blood concentration time profiles are maintained, reducing negative effects.
8. Medication release that lasts for a long period after application, extending the duration of the activity.
9. Utilized are medications having limited biological half-lives and therapeutic windows.
10. Preventing the volatility of drug plasma levels.
11. Potent medications' plasma concentration is kept constant.
12. Therapy may be stopped at any moment with ease.

13. Getting rid of the conventional multiple-dosing profile will improve patient compliance.

14. Transdermal route is utilized as an alternative to administer the medication candidate when oral route is problematic, such as with vomiting and diarrhea.

LIMITATIONS FOR SELECTION OF TDDS:

Not all medications may be delivered this way; the medication must possess certain beneficial physicochemical features.

- Unsuitable for medications that call for high plasma levels.
- Unsuitable for medications that cause contact dermatitis and skin rashes.
- Incompatible with medications with high molecular weight.
- Unsuitable for medications that are metabolized as they go through the skin.
- Since the skin is a particularly effective barrier to drug penetration, a substantial variety of medications cannot be administered by the transdermal method. Only a little dosage may be given.

PHYSIOLOGY OF THE SKIN:

A typical adult's skin has a surface area of around 2 m^2, and it gets roughly one-third of the blood that circulates through the body. The topmost layer of skin, the epidermis, includes four morphologically different regions: the basal layer, the spiny layer, the stratum granulosum, and the highest stratum corneum. The epidermis is made up of highly cornified (dead) cells that are continuously encased in a matrix of lipid membrane sheets. Ceramides, cholesterol, and free fatty acids make up the special makeup of these extracellular membranes. Every square centimeter of human skin is known to have between 200 and 250 sweat ducts and 10 to 70 hair follicles on average. It is one of the human organs that is easiest to reach.

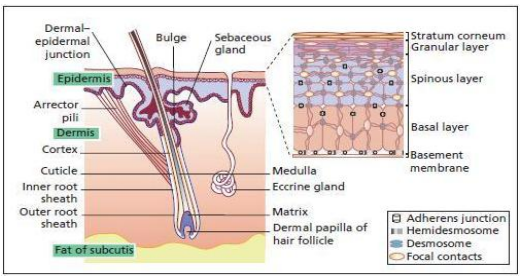

Figure 1: Anatomical and physiological Structure of skin

SKIN PATHWAYS FOR TRANSDERMAL DRUG DELIVERY SYSTEMS:

Drugs may penetrate and pass through the skin in a number of ways when administered to the skin's surface. Drugs may enter the body either transepidermally (transepidermal) or transappendageally (transappendageal) (Figure 2). There are two distinct ways to penetrate the stratum corneum: (1) via the corneocytes and lipid lamellae alternately (trans cellular route); and (2) following the winding channel between the lipid lamellae (intercellular route)

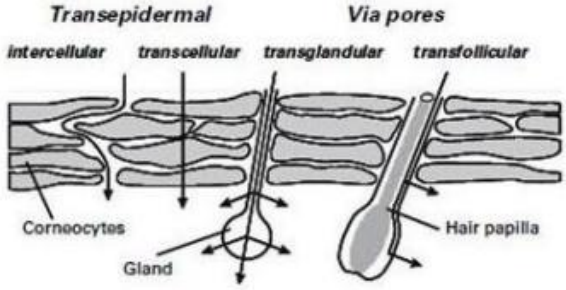

Figure 2: Possible pathways for permeation of drug across the skin barrier

It is generally acknowledged that the intercellular pathway is the most common way

to penetrate the stratum corneum. The heavily cross-linked cornified membrane covering the keratinocytes is mostly to blame for this. Water and other tiny hydrophilic molecules cannot entirely be eliminated from trans cellular transit, nevertheless. The eccrine sweat gland duct or the follicular duct are both included in the appendage route or shunt route. While the follicular duct contains mostly lipophilic material, the eccrine sweat glands are mostly hydrophilic. Sebum that is excreted into the follicular duct entrance is mostly to blame for this. It is well acknowledged that intact stratum corneum serves as the primary conduit for passive skin permeation because of its enormous surface area.

FACTORS INFLUENCING TRANSDERMAL DRUG DELIVERY:

Three elements drug, skin, and delivery vehicles can be combined to create an efficient transdermal drug delivery system. Therefore, the influencing elements may be classified as biological factors and physicochemical factors.

A. Biological factors:

Skin condition: Acids, alkalis, and several solvents, including chloroform and methanol, harm skin cells and encourage penetration. Patient illness affects their skin's condition. Although the undamaged skin serves as a superior barrier, the aforementioned circumstances limit penetration.

Skin age: Younger skin is more porous than older skin. Children are more susceptible to toxin absorption via the skin. Consequently, one of the parameters influencing medication penetration in TDDS is skin age.

Blood supply: Transdermal absorption may be impacted by changes in peripheral circulation.

Localized skin site: Site differences include differences in appendage density, stratum corneum type, and skin thickness. These elements have a big impact on penetration.

Skin metabolism: Steroids, hormones, chemical carcinogens, and certain medicines are all processed by the skin. Therefore, skin metabolism influences how well a medicine penetrates the skin.

Species differences: The penetration is affected by the thickness, density, and keratinization of the skin, which differ from species to species.

B. Physicochemical factors:

Skin hydration: The permeability of skin rises dramatically when it comes into touch with water. The most crucial aspect in promoting skin permeability is hydration. Humectants are therefore used in transdermal distribution. pH and temperature: With temperature change, medication penetration increases tenfold. As temperature drops, the diffusion coefficient lowers. Depending on the pH and pKa or pKb values, weak acids and bases separate. The drug concentration in skin is based on the percentage of unionized drug. Consequently, crucial variables impacting medication penetration include temperature and pH.

Diffusion coefficient: Drug diffusion coefficient affects drug penetration. The features of the drug, the diffusion medium, and their interactions determine the drug's diffusion coefficient at a constant temperature.

Drug concentration: The flow is inversely correlated with the gradient of concentration across the barrier, and the gradient will be bigger if the drug concentration is higher across the barrier.

Partition coefficient: For effective action, the ideal K, partition coefficient is necessary. High K drugs are not yet ready to exit the lipid layer of skin. Additionally, low-K medicines won't penetrate the body.

Molecular size and shape: Small molecules enter more quickly than big ones, thus the relationship between molecular weight and drug absorption is inverse. The impact of molecule size is unknown because to partition coefficient dominance.

TYPES OF TRANSDERMAL PATCHES

Single layer drug in adhesive: In this form, the medicine is included in the sticky layer. The adhesive layer is in charge of delivering the medicine onto the skin in addition to holding the other layers together. There is a backer and a temporary liner around the adhesive layer.

Multi -layer drug in adhesive: This kind is similar to the single layer in that it also has an instant drug release layer, a controlled release layer, and an adhesive layer. The sticky layer is in charge of the drug's release. Additionally, this patch features a long-lasting backing and a temporary liner layer.

Vapour patch: The adhesive layer's function in this kind of patch goes beyond just holding the several layers together. It also functions as a market, which is often utilized to release essential oils during decongestion. There are many different kinds of vapor patches on the market that are designed to enhance sleep quality and lessen the effects of smoking.

Reservoir system: In this method, a membrane that controls the flow rate is sandwiched between an impermeable backing layer and a drug reservoir. Only via the rate-regulating membrane, which may or may not be microporous, does the medication release. The medication might be in a solution, suspension, gel, or distributed in a solid polymer matrix in the drug reservoir compartment. A polymeric membrane with an outside surface that is hypoallergenic and compatible with drugs may be used.

CONCLUSION

Delivering regular dosages of numerous drugs through transdermal drug administration is painless, practical, and perhaps successful. Improved medication absorption and delivery of a wide variety of medicines minimal difficulties, negative effects, cheap cost, and simplicity of usage. An authorized therapeutic product that is now administered orally may be delivered trans dermally to bypass first pass metabolism. The most popular way to give medications trans dermally is through dermal patches. However, because of the relatively impermeable thick outer stratum corneum layer, transdermal technologies are constrained. Transdermal Patches have also made significant advancements. In addition, there are a number of additional obstacles that prevent the widespread adoption of TDDS and its guaranteed effectiveness, making study in this field challenging. For instance, the skin is an extremely complex and difficult barrier for medications to pass through and enter the blood.

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