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TRANSDERMAL DRUG DELIVERY SYSTEM: AN OVERVIEW

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Abstract
Transdermal drug delivery system (TDDS) is topically administered dosage form in the form of patches which deliver drugs for systemic effects at a predetermined and controlled rate. This review focuses towards the basic facts about the transdermal drug delivery system. including the methods of their preparation and some of the recent advancements that have in achieved this promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication delivery such as oral topical, intravenous. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. Transdermal drug delivery offers controlled release of the drug into the patient, it enables a steady blood level profile, resulting in reduced systemic side effects.

Keywords : Transdermal Drug Delivery System, skin, transdermal patch

Introduction

The transdermal drug delivery system (TDDS) is one of the systems lying under the category of controlled drug delivery, in which the aim is to deliver the drug through the skin at a predetermined and controlled rate. TDDS are adhesive drug-containing devices of defined surface area that deliver a predetermined amount of drug to the surface of intact skin at a programmed rate to reach the systemic circulation.

Transdermal delivery provides a leading-edge over injectables and oral routes by increasing patient compliance and avoiding first-pass metabolism, respectively. The transdermal route has vied with oral treatment as the most successful innovative research area in drug delivery, as oral treatment involves attainment and maintenance of drug concentration in the body within a therapeutically effective range by the introduction of a fixed-dose at regular intervals, due to which the drug concentration in the body follows a peak and trough profile, leading to a greater chance of adverse effects or therapeutic failure; a large amount of drug is lost in the vicinity of the target organ and close attention is required to monitor therapy to avoid overdosing. The limitations of the oral route can be overcome and benefits of intravenous drug infusion such as bypassing hepatic "first pass" hepatic elimination (HEPE) to maintain constant prolonged and therapeutic effective drug levels in the body can be closely duplicated, without its potential hazards, by transdermal drug administration through intact skin.[1]

Advantages

1. Suitable for drug candidates with a short half-life and low therapeutic index.
2. No first-pass effect.
3. Reduction in dosing frequency.
4. Minimization of daily intake of the drug.
5. Reduction of fluctuations in plasma drug concentration.
6. Improves patient compliance.
7. Minimization of side effects.
8. Simple and non-invasive.
9. An alternate route for patients who are unable to take oral medications.
10. Dose delivery unaffected by vomiting or diarrhea.
11. Drug administration stops with patch removal. [1]

Disadvantages

1. The transdermal route of administration is unsuitable for drugs that irritate or sensitize the skin.
2. Only relatively potent drugs are suitable for transdermal delivery due to the natural limits of drug entry by the skin's impermeability.
3. Technical difficulties with the adhesion of the systems to different skin types and under various environmental conditions.
4. A constant concentration gradient is difficult to maintain.[1]

Benefits of TDDS

1. Transdermal medication provides safe, convenient and pain-free self-administration for patients.
2. Transdermal delivery may be useful in those patients who are polymedicated.
3. Transdermal drug delivery provide a constant rate of release of medicine tomaintain concentration level of drug for a longer period of time as to avoid peak and valley associated with oral dosing and parenteral administration.
4. Transdermal patches improved therapeutic effect s of various drugs by avoiding specific problems associated with drugs such as presystemicmetabolism,formation of toxic metabolites, low absorption,gasto intestinal irritation etc.
5. Useful in drugs possesses short half-life as to avoid frequent dosing administration. 6. Reduced inter & intra – patient variability by simplified medication regimen.
7. Greater advantage in those patients who are unconscious, dysphagia or constipation.
8. Elimination of pre-systemic metabolismresult in reduction the amount of drug administered, resulting in the reduction of adverse effects and hence safer in hepato-compromised patients.
9. Fruitful in especially when long-term treatment is required, as in chronic pain treatment e.g. hormone replacement etc. and smoking cessation therapy.
10. The drug input can be terminated at any point of time by removing transdermal system.
11. Transdermal systems are generally inexpensive and economic when compared with other therapies on cost basis, as patches are designed to deliver drugs from 1 to7 day.[2]

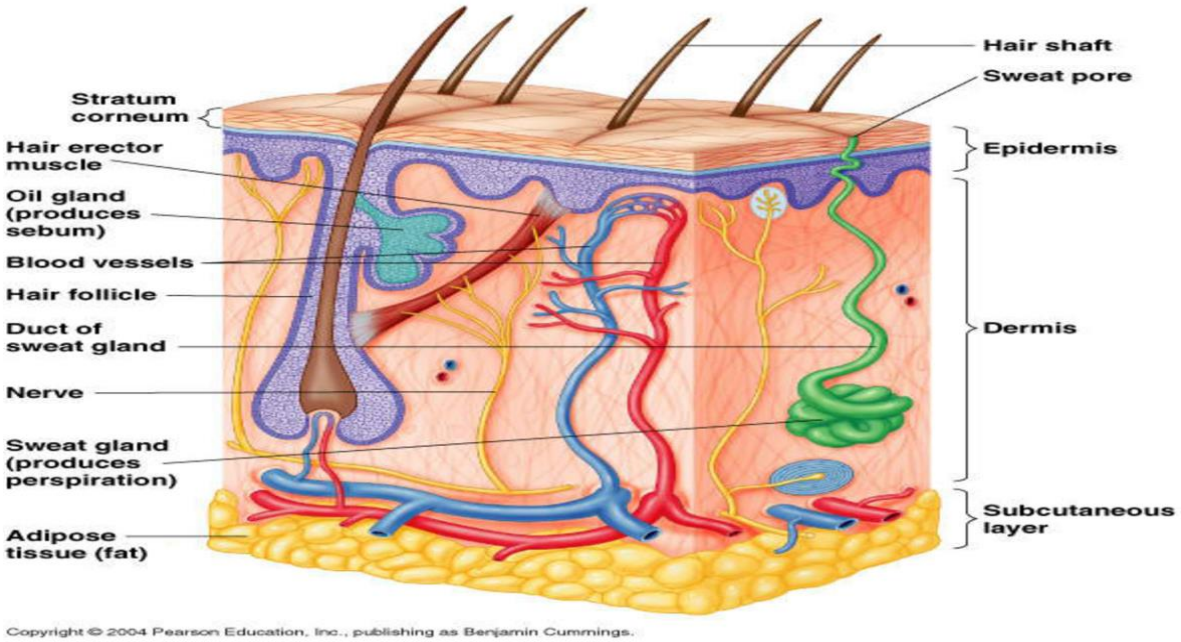

Fig No 01: Structure of skin

Types of transdermal patches[3]

a) Single layer drug in adhesive: In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and also responsible for the releasing the drug to the skin.

b) Multi -layer drug in adhesive: This type is also similar to the single layer but it contains an immediate drug release layer and other layer will be a controlled release along with the adhesive layer. The adhesive layer is responsible for the releasing of the drug. This patch also has a temporary liner-layer and a permanent backing.

c) Vapour patch: In this type of patch the role of adhesive layer not only as release vapour. The vapour patches are new to the market, commonly used for releasing of essential oils in decongestion. Various other types of vapor patches are also available in the market which are used to improve the quality of sleep and reduces the cigarette smoking conditions.

d) Reservoir system: In this system the drug reservoir is embedded between an impervious backing layer and a rate controlling membrane. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix.

Skin Permeation

The skin is the largest organ of the body. The skin an average adult body is about 20 square feet and it received about one third of total available blood. The skin is multilayered organ composed of three histological tissue:

- the outermost layer of skin,epidermis is which provides a waterproof barrier and creates our skin tone.
- dermis, beneath epidermis, contains tough connective tissue, hair follicles, and sweat glands and
- deeper subcutaneous tissue (hypodermis) is made of fat and connective tissue.[4]

There are main three pathways through which foreign particles diffused or penetrate in to skin:

1. Transcellular/Intracellular permeation through the stratum corneum
2. Intercellular permeation through the stratum corneum
3. Transappendageal permeation via the hair follicles, sweat and sebaceous gland[5]

Mechanism of transdermal permeation:

Transdermal permeation of a drug moiety involves the following steps:

i. Sorption by stratum corneum

ii. Permeation of drug through viable epidermis
iii. Uptake of the drug moiety by the capillary network in the dermal papillary layer.
iv. The drug must possess some physicochemical properties to reach target site via systemically through stratum corneum.[6]

Basic components of TDDS

Polymer matrix / Drug reservoir:
• Drug
• Permeation enhancers
• Pressure sensitive adhesive (PSA)
• Backing laminates
• Release liner
• Other recipients like plasticizers and solvents[7]

Polymer matrix / Drug reservoir: Polymers are the backbone of TDDS, which control the release of the drug from the device. Polymer matrix can be prepared by dispersion of drug in liquid or solid state synthetic polymer base. Polymers used in TDDS should have biocompatibility and chemical compatibility with the drug and other components of the system such as penetration enhancers and PSAs.

Drug: The Transdermal route is an extremely attractive option for the drugs with appropriate pharmacology and physical chemistry. Transdermal patches offer much to drugs which undergo extensive first pass metabolism, drugs with narrow therapeutic window, or drugs with short half life which causes non- compliance due to frequent dosing. the drugs for Transdermal delivery. In addition drugs like rivastigmine for Alzheimer's and Parkinson dementia, retightened for Parkinson, methylphenidate for attention deficit hyperactive disorder and elegizing for depression are recently approved as TDDS.

Permeation Enhancers: These are the chemical compounds that increase permeability of stratum corneas so as to attain higher therapeutic levels of the drug candidate.Penetration structural components of stratum conium i.e., proteins, lipids. They alter the protein and lipid packaging of stratum conium, thus chemically modifying the barrier functions leading to increased permeability.

Pressure sensitive adhesives: A PSA is a material that helps in maintaining an intimate contact between Transdermal system and the skin surface. It should adhere with not more than applied finger pressure, be aggressively and permanently tacky, exert a strong holding force. Additionally, it should be removable from the smooth surface without leaving a residue. Polyacrylates, polyisobutylene and silicon based adhesives are widely used in Todd's.

Release Liner: During storage the patch is covered by a protective liner that is removed and discharged immediately before the application of the patch to skin. It is therefore regarded as a part of the primary packaging material rather than a part of dosage form for delivering the drug.

Other excipients: Various solvents such as chloroform, methanol, acetone, isopropanol and dichloromethane are used to prepare drug reservoir. In addition, plasticizers such as polyethylene glycol and propylene glycol are added to provide plasticity to the transdermal patch.[8-16]

Factors affecting TDDS

A. Biological factor

1) Skin conditions The intact skin itself acts as barrier but many agents like acids, alkali cross the barrier cells and penetrates through the skin, many solvents open the complex dense structure of horny layer Solvents like methanol, chloroform remove lipid fraction, forming artificial shunts through which drug molecules can pass easily.
2) Skin age: It is seen that the skin of adults and young ones are more permeable than the older ones but there is no dramatic difference. Children shows toxic effects because of the greater surface area per unit body weight. Thus potent steroids, boric acid, hexachlorophene have produced severe side effects.
3) Blood Supply: Changes in peripheral circulation can affect transdermal absorption.
4) Regional skin site: Thickness of skin, nature of stratum corneum and density of appendages vary site to site. These factors affect significantly penetration.
5) Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens and some drugs. So skin metabolism determines efficacy of drug permeated through the skin.

6) Species differences: The skin thickness, density of appendages and keratinization of skin vary species to species, so affects the penetration.

B. Physicochemical factors

1) Skin hydration In contact with water the permeability of skin increases significantly. Hydration is most important factor increasing the permeation of skin. So use of humectant is done in transdermal delivery.

2) Temperature and pH The permeation of drug increases ten folds with temperature variation. The diffusion coefficient decreases as temperature falls. Weak acids and weak bases dissociate depending on the pH and pKa or pKb values. The proportion of unionized drug determines the drug concentration in skin. Thus, temperature and pH are important factors affecting drug penetration.

3) Diffusion coefficient Penetration of drug depends on diffusion coefficient of drug. At a constant temperature the diffusion coefficient of drug depends on properties of drug, diffusion medium and interaction between them.

4) Drug concentration The flux is proportional to the concentration gradient across the barrier and concentration gradient will be higher if the concentration of drug will be more across the barrier.

5) Partition coefficient The optimal partition coefficient (K) is required for good action. Drugs with high K are not ready to leave the portion of skin. Also, drugs with low K will not be permeated.

6) Molecular size and shape Drug absorption is inversely related to molecular weight; small molecules penetrate faster than large ones.

C. Environmental factors

1) Sunlight Due to Sunlight the walls of blood vessels become thinner leading to bruising with only minor trauma in sun-exposed areas. Also pigmentation: The most noticeable sun-induced pigment change is a freckle or solar lentigo.

2) Cold Season often result in itchy, dry skin. Skin responds by increasing oil production to compensate for the weather's drying effects. A good moisturizer will help ease symptoms of dry skin. Also, drinking lots of water can keep your skin hydrated and looking radiant.

3) Air Pollution: Dust can clog pores and increase bacteria on the face and surface of skin, both of which lead to acne or spots. This affects drug delivery through the skin. Invisible chemical pollutants in the air can interfere with skin's natural protection system, breaking down the natural skin's oils that normally trap moisture in skin and keep it supple.

4) Effect of Heat on Transdermal patch: Heat induced high absorption of transdermal delivered drugs. Patient should be advised to avoid exposing the patch application site to external heat source like heated water bags, hot water bottles. Even high body temperature may also increase the transdermally delivered drugs.[8-16]

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