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Transdermal Drug Delivery System

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Abstract

(TDDS) additionally called ‘ Transdermal patches,’ square measures dose form design to deliver a The human skin is readily accessible surface for drug delivery. Transdermal Drug Delivery Systems therapeutically effective quantity of drug across a patients skin. In order to deliver therapeutics agents through the human skin for systemic effect, the comprehensive morphological , biophysical and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patients compliance and avoiding first pass metabolism respectively. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulse entry into systemic circulation, which often causes undesirable side effects. Over the past decades, developing controlled drug delivery has become increasingly important in the pharmaceutical industry. The human skin surface is known to contain, on an average,10-70 hair follicles and 200-250 sweat duct on every square centimeters of the skin area. Skin penetration enhancement techniques have been developed to improve bioavailability and increase the range of drugs for which topical and transdermal delivery is viable option. The present review article explores the overall study on transdermal drug delivery (TDDS) which leads to novel drug delivery system(NDDS).

Keywords: Transdermal drug delivery system, Skin anatomy, polymer matrix,evaluation parameter, future of transdermal therapy

Introduction

Transdermal patch (skin patch) uses a special membrane to control the rate at which the liquid drug contained in reservoir within the patch can pass through the skin and into the bloodstream. Developing controlled drug delivery has become increasingly important in the pharmaceutical industry. Tablets and injections have been the traditional way to take medications; new options are increasingly popular. One transdermal highly successful alternative delivery method is the transdermal. Drugs administered through skin patch include scopolamine (for motion sickness), nicotine for (quitting smoking), estrogen (for menopause and to prevent osteoporosis after meno pause), nitroglycerin (for angina), and lidocaine to relieve the pain of shingles (herpes zoster). Molecule of insulin and many other substances, however, are too large to pass through the skin. Transdermal patch were developed in 1970s and the first was approved by the FDA in1979 for the treatment of motion sickness. [1,2] it was a three day patch that delivered scopolamine. Transdermal patches have been useful in developing new applications for existing therapeutics and for reducing first-pass drug-degradation effects.

- DEFINITION :A transdermal patch or skin patch is a medicated adhesive patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through skin and into the bloodstream

Transdermal drug delivery (TDD) :-The usage of intact skin as a portal of entry for drugs into the systemic circulation attracted tremendous interest after the introduction of the first dermal patch containing scopolamine. Transdermal drug delivery is a viable administration route for potent, low molecular weight therapeutics agents which cannot withstand the hostile environment of the gastrointestinal tract and/ or are subjects to considerate first pass metabolism by the liver.

The release of a drug from the formulation applied to the skin surface and its subsequent transport to the systemic circulation involves several steps :

1. Dissolution within and release from the formulation,
2. Partitioning into the skins outermost layer ,the stratum corneum (SC),
3. Diffusion through the SC, principally via a lipidic intercellular pathway,
4. Partitioning from the SC into the aqueous viable epidermis,
5. Diffusion through viable epidermis and into the upper dermis, and
6. Uptake into the local capillary network and eventually the systemic circulation.

- **ADVANTAGES**

  - Topical patches are easier to use and remember.
  - Drug therapy may be terminated rapidly by removal of the application from the surface of the skin
  - Topical patches are cost effective.
  - They can avoid gastrointestinal drug absorption difficulties covered by gastrointestinal pH,enzymatic activity and drug interaction with food,drink and other orally administration drug
  - Topical patches have fewer side effects so mostly peoples prefer this.

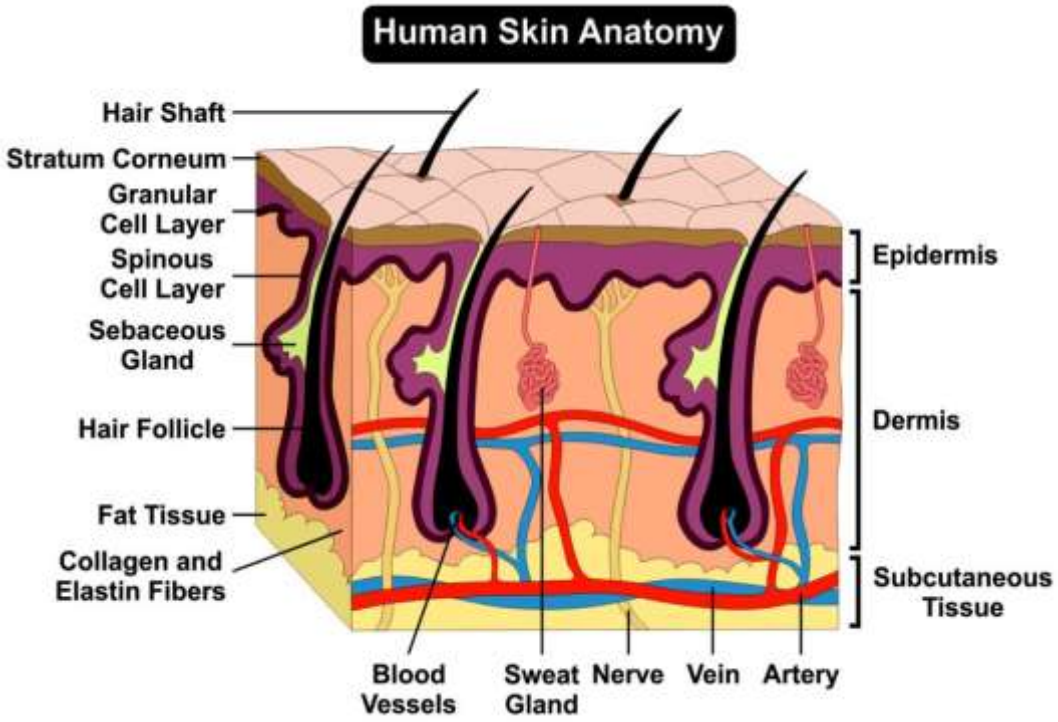
- **DISADVANTAGE**

  - The adhesives may not adhere well to all types of skin and may be uncomfortable to wear.
  - Only potent drugs are suitable candidates for transdermal patch because of the natural limit of drug entry imposed by skins impermeability.
  - Some drugs e.g. scopolamine transdermal patch placed behind the ear, it is uncomfortable.
  - LIMITATIONS
  - TDDS cannot deliver ionic drugs.
  - TDDS cannot develop if drug or formulation causes irritation to skin.
  - It cannot develop for drugs of large molecular size.
  - TDDS achieve high drug levels in blood/plasma

Anatomy of skin:Skin is the largest organ of the human body, covering a surface area of 2 m^2 and receiving one-third of the total blood supply. Human skin comprises of three distinct but mutually dependent tissues :

- The stratified, vascular, cellular epidermis,

- Underlying dermis of connective tissues and
- hypodermis



Epidermis

The multilayered epidermis varies in thickness, depending on cell size and number of cell layers of epidermis, ranging from 0.8 mm on palms and soles down to 0.06 mm on the eyelids. it consists outer stratum corneum and viable epidermis.

a) Stratum corneum :
This is outermost layer of skin also called as horney layer . it contains 10 to 25 layers of dead, keratinized cells called corneocyctes. It is flexible but relatively impermeable. The architecture of horney layer may be modeled as a wall-like structure. In this model , the keratinized cells function as a protein “bricks” embedded in lipid “mortar.” The lipids are arranged in multiple

b) Viable epidermis :
This is situated beneath the stratum corneum and varies in thickness from 0.06mm on the palms. It consists of various layers as stratum spinosum,stratum basal, stratum granulosum and stratum lucidum. In the basal layer, mitosis of the cells constantly renews the epidermis and this proliferation compensates the loss of dead horney cells from the skin surface.

Dermis

Dermis is 3 to 5mm thick layers and is composed of a matrix of connective tissues, which contains blood vessels lymph vessels and nerves. The cutaneous blood supply has is essential function in regulation of body temperature. It also provides nutrients and oxygen to the skin while removing toxins and waste products. The blood supply thus keeps dermal concentration of a permanent very low and the resulting

concentration difference across the epidermis provides the essential concentration gradient for transdermal permeation.

Hypodermis

The hypodermis or subcutaneous fat tissue supports the dermis epidermis. It serves a fat storage area. This layer to regulate temperature, provides nutritional support and mechanical protection. Its carriesprinciple blood vessels and nerves to skin and may contain sensory pressure organs.

Components of transdermal patches

- Polymer matrix :The polymer controls the release of the drug from the device. The following criteria should be satisfied for a polymer to be used in transdermal patches.

✓ The polymer should be nontoxic.
✓ The polymer should be inexpensive.
✓ Molecular weight, functionality of the polymer should be such that the specific drug diffuses properly and gets released through it.
✓ The polymer should be stable.
✓ Large amounts of the active agent are incorporated into it.
✓ The polymer should be easily of manufactured.

Types of polymer :-

➢ Natural polymer : Cellulose derivatives, gelatin, waxes, proteins, shellac, natural rubber, starch.
➢ Synthetic elastomers : hydrin rubber, silicone rubber, nitrile, acrylonitrile, neoprene
➢ Synthetic polymers : polyvinyl alcohol, polyvinyl chloride, epoxy, polypropylene.

- Drug :Drug solution in direct contact with release liner.

Physiochemical properties:-

a. The drug should have a molecular weight less than 1000 daltons.
b. The drug should have infinity for both lipophilic and hydrophilic phases.
c. The drug should have a low melting point.

Biological properties :-

a. The drug should be potent with a daily dose of the order of a few mg/day.
b. The half life of the drug should be short.
c. The drug must not produce allergic response.
d. Tolerance to the drug must not develop under the near zero-order release profile of transdermal patches.

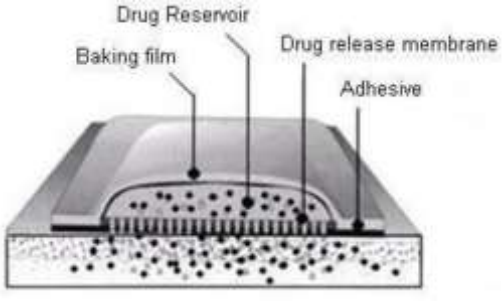


Fig. 2 : Different parts of transdermal patch

- Permeation enhancer :- The flux J. of drugs across the skin can be write As
- J= D dc/dx
- J= the Flux
  D= diffusion coefficient
  C= concentration of the diffusing spectes
  X= Spatial coordinate

a) Solvent :- These compounds increase penetration possible by swelling the polar pathway.
e.g. water alcohols- Menthol& ethanol, / Dimethyl acetamide Propylene glycol and Glycerol.
b) Surfactants- The ability of a surfactant to alter penetration is a function of the polar head group and the hydrocarbon chain length.
c) Miscellaneous chemicals :- these include urea , a hydrating and keratolytic agent; N, N dimethyl-m-toluamide; calcium thioglycolate; anticholinergic agents.
d) Enhance the permeation e.g. urea, calcium thioglycolate.

- Other excipients :- Adhesives–The pressure sensitive adhesive can be positioned on the face of the device or in the back of the device.
  - It should not be irritant
  - It should be easily removed
  - Permeation of drug should not effected
  - Physically and chemically compatibility with the drug
- Linear :- Protect the patch during storage. The linear is removed prior to use.
- Backing :- Protect the patch from the outer environment. The backing layer should be impermeable to drug and penetration enhancer. Serves a function of holding the entire system and protect drug reservoir from atmosphere.

Types of Transdermal patches :

1. Single layer drug in adhesive :In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layer together and also responsible for the releasing the drug to the skin.
2. Multiple-layer drug in adhesive : This type is also similar to the single layer but it contains a immediate drug release layer and other layer will be a controlled release along with the adhesive layer.
3. Vapour patch : In this type of patch the role of adhesive layer not only serves to adhere the various layer together but also serves market, commonly used for releasing of essential oils in decongestion.
4. Reservoir system : In this system the drug reservoir is embedded between an imperious backing layer and a rate controlling membrane. The drug release only through the rate controlling membrane, which can be micro porous or non porous.
5. Microreservoir system : In this type the drug delivery system is a combination of reservoir and matrix-dispersion system. The drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer and the dispersing the solution homogenously in a lipophilic polymer to form thousand of unreachable, microscopic spheres of drug reservoirs.

Evaluation parameters :

1. Interaction studies
2. Water vapour permeability (WVP) evaluation
3. Weight uniformity
4. Folding endurance
5. Drug content
6. Flatness test
7. Skin irritation study
8. Thumb tack test
9. Percentage moisture content
10. In vitro drug release studies
11. In vitro skin permeation studies
12. Rolling ball tack test
13. Thickness of the patch
14. Shear adhesion test
15. Peel adhesion test

Future of Transdermal Therapy

Ten years ago, the nicotine patch had revolutionized smoking cessation ; patients were being treated with nitroglycerine for angina, clonidine for hypertension, scopolamine for motion sickness and estradiol for estrogen deficiency, all through patches. At that time, biotech medicinal was still being developed. During the past decade, the number of drugs formulated in the patches has hardly increased, and there has been little change in composition of the patch system.

Modification have been mostly limited to refinements of the material used. The reason is the only limited number of drugs fit the molecular weight, potency requirement for transdermal absorbtion.

Conclusion

This review provide an valuable information regarding the transdermal drug delivery systems and its evaluation process details as a ready reference for the research scientist who are involved in TDDS. However, without greater understanding of the structure and function of skin. The various types of transdermal patches and its advantages, disadvantages and few limitations. The properties of the drug, the characteristics of the transdermal device, selection of in-vivo model and the status of patients skin are all important for safe and effective drug delivery. The transdermal drug delivery system could be one day one of the best novel drug delivery system.

References

1. Shaila L, Pandey S and Udupa N. Design and evaluation of matrix Type membrane controlled Transdermal Drug Delivery System of Nicotin suitable for use in smoking cessation. Indian journ. Pharm. Sci. 2006;68: 179-184
2. Tortara GS, Grabowski SK. Principle of Anatomy, Nineth edition, 2000, pp 140-194.
3. Bodae HW, De Hnn FHN. Drug permeation enhancement : Theory and Application, In :
4. Hsieh DS editor, Drugs and Pharmaceutical Sciences, New York : Marcel Dekker, 1994, 62, pp 59-90.

5. Zhang Q, Shen Z, Nagai T. prolonged hypoglycemic effect of insulin-loaded polybutylcyanoacrylate nanoparticles after pulmonary administration to normal rats. Int. J. Pharm. 2001; 218: 75-80.
6. Rhaghuram RK, Muttalik S, Reddy S. Once-Daily sustained- Release Matrix Tablets of Nicorandil : formulation and Invitro Evaluation. Aaps Pharm.Scitech. 2003; 4(4) : 480-488.
7. Baker W and Heller J. Material selection for Transdermal Delivery Systems. In Transdermal Drug Delivery : Development Issues and Research Initiatives, J.Hadgraft and R.H.Guys, Eds. Marcel Dekker, Inc., New York. 1989Pp. 293-311.
8. Finnin, B C, and T M Morgan. 1999. "Transdermal Penetration Enhancers: Applications, Limitations, and Potential." Journal of pharmaceutical sciences 88 (10): 955-58.
9. http://www.ncbi.nlm.nih.gov/pubmed/10514338.
10. Cevc, Gregor. 1997. "Drug Delivery across the skin." Expert opinion on investigational Drugs 6(12): 1887-1937. Doi:10.1517/13543784.6.12.1887.
11. Brown, Marc B., Gary P . Martin, Stuart A. Jones, and Franklin K. Akomeah. 2006. "Dermal and Transdermal Drug Delivery Systems: Current and Future Prospects." Drug Delivery 13 (3). Taylor & Francis: 175-87. doi: 10.1080/107540500455975.
12. "TRANSDERMAL DRUG DELIVERY SYSTEM." n.d. https://www.slideshare.net/GajananSanap/transdermal-drug-delivery-58779074.
13. Vyas SP, Khar RK. Controlled Drug Delivery: Concepts and Advances, first edition, Vallabh Prakashan, 2002, pp 411-447.
14. Images [Internate] URL, : http/Google.com/images.
15. Zhou Y, Wu XY. Fine element analysis of diffusional drug release from complex matrix system, J control Rel 1997; 49: 277-288.
16. Pellet M, Raghavan S.L, Hadgraft J and DavisA.F. "The application of supersaturated systems to percutaneous drug delivery" In : Guy R.H and Dekker, Inc, New York 2003, pp. 305-326.
17. Berner b, John VA. Pharmacokinetic characterization of Transdermal delivery system. Jour. Clinical pharmacokinetics 1994; 26(2): 121-34.
18. Allen LV, Popovich NG, Ansel HC. Pharmaceutical dosage form and drug delivery systems, seventh edition, Lippincott Williams and Wilkins, 2002, 263-278.
19. Ryan D. Gordon, and Tim A. Peterson, Transdermal Drug Delivery, Drug Delivery Technology. www.Drugdeliverytechnology.Com.
20. Sakalle P, Dwivedi S and Dwivedi A. Design, Evaluation, Parameters and Marketed Porducts of Transdermal Patches: A Review. Journal of Pharmacy Research. 2010; 3 (2): 235-240.
21. Williams, Adrian C, and Barry 2004, "Penetration Enhancers." Advanced Drug Delivery Reviews 56 (5): 603-18. doi: 10.1016/j.addr.2003.10.025.
22. Wang, Yiping, Rashmi Thakur, Qiuxi Fan, and Bozena Michniak. 2005. "Transdermal Iontophoresis: Combination Strategies to Imporve Trandsermal Iontophoretic Drug Delivery." European Journal of Pharmaceutics and Biopharmaceutics 60(2): 179-91. doi: 10.1016/j.ejpb.2004.12.008.