International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 864-869 www.ijprajournal.com ISSN: 2456-4494

Transdermal Drug Delivery System: An Overview

Chouhan Nidhi, Gupta Ashish*, Sharma Ravi, Sharma Pravin K., Mahajan Shraddha, Darwhekar Gajanan

Acropolis institute of pharmaceutical education and research, Indore, Madhya Pradesh 453771

Submitted: 15-05-2022 Revised: 25-05-2022 Accepted: 28-05-2022

ABSTRACT:
This review article complies all the work on transdermal drug delivery system have generated extensive interest as preferred alternative to oral drug delivery system. Transdermal drug delivery system can offer a controlled release of the drug through the skin. The field of transdermal drug delivery system aimed at developing safe and efficacious means of delivering medication across the skin. Transdermal patch also allow for fast interruption of the treatment in the case of any adverse effect. Textile materials are often permeable, comfortable, aesthetic, breathable structure. The benefits of using transdermal drug delivery include avoid the gastrointestinal tract and bypasses first pass metabolism. The limitations of transdermal drug delivery is long time adhere is difficult and it cannot develop for drug of large molecular size. The present review articles explore the overall study on transdermal drug delivery system which leads to novel drug delivery system.

Keywords: Transdermal drug delivery, Skin permeation, Pharmacokinetics, Reservoir system, Polymer matrix, Permeation enhancers.

I. INTRODUCTION:

Transdermal Drug Delivery System

Around 74% of drugs are taken orally today and are found not to be as efficient as desired. To enhance certain transdermal drug characteristics there was a delivery system. Drug delivery through the skin is usually referred to as transdermal to achieve a systemic effect of a drug. Transdermal drug delivery systems (TDDS) provide modes of dosage that include for local therapeutic effect, the transport of drugs to viable epidermal and dermal skin tissues as well as a very large fraction of the drug is transported into the circulation of systemic blood. The (TDDS) adhesive is essential for safety, effectiveness, and Product efficiency and quality.

Transdermal drug delivery systems are the route of administration through which a drug is given into systemic circulation by Passover the natural barrier that intact skin poses. The TDDS has been around for a while now. The 1st TDDS, which was a Scopolamine patch, the US FDA has approved it in 1979 for motion sickness care. Many other items have then been accepted that supplied drugs including clonidine, nitroglycerin, fentanyl and estradiol.

Pharmacokinetics of transdermal drug delivery:

The drug needs to be present in a high concentration within the patch for transdermal delivery to occur. The energy for drug release is derived from the concentration gradient existing between a saturated solution of the drug in the system and the much lower concentration in the skin; drug movement occurs by diffusion. Since there is a high concentration within the patch and allow concentration in the blood, the drug will continue to diffuse, maintaining a constant concentration of the drug in the circulation.

Benefits of Transdermal Drug Delivery System:

- Non-invasive route, quick and simple to terminate.
- Bypass first-pass metabolism and no dosing-related food effects.
- Eliminates the need for regular dosing, once daily or multi-day patches those are easy to achieve.
- Low dose-dumping risk.
- Acceptable for pediatrics, unconscious and geriatric populations.
- Easier to use and remember.
- Minimizing undesirable side effects.
- Avoid gastro intestinal incompatibility.

Limitations of Transdermal Drug Delivery System:

- Risk of inflammations on the skin.
- Ionic drug cannot be administered.
- Long time adhere is difficult.
- It cannot develop for drug of large molecular size.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 864-869 www.ijprajournal.com ISSN: 2456-4494

- TDDS cannot develop if drug or formulation causes irritation to skin.
- Drug size more than 500 Dalton are not suitable for TDDS.
- Difficult to administer the large dose more than 10 mg/day.

Factors affecting transdermal patch:

Physicochemical property:

- Partition coefficient
- Molecular size ionization
- Solubility
- Melting point

Physiological and pathological property:

- Reservoir effect
- Lipid film
- Skin hydration
- Regional variation
- Coetaneous self metabolism
- Skin barrier properties in the neonate and young infant
- Body site. [4, 5]

Basic principle of transdermal permeation:

Transdermal permeation is based on passive diffusion skin is the most intensive accessible organ of the body as only a fraction of millimeters of tissue separates surface from the underlying capillary network.

The release of a therapeutic agent from a preparation fix to the skin surface and it convey to the systemic circulation is a multistep process, which is discussed below:

- Diffusion of medication from the drug formulation to the rate controlling membrane.
- Dissolution occurs inside, and release from the formulation.
- Sorption by layer conium and penetration through viable epidermis.
- Uptake of medication by capillary network in the dermal papillary layer.
- Effect on the objective / target organ.
- Partitioning into the skins' outer most layer, the stratum conium.
- Dissolution through the layer conium, principal trough a lipid intercellular pathway.

Types of Transdermal Drug Delivery System:

Single Layer Drug in Adhesive: The adhesive layer contains the medication in this form. The adhesive layer not only binds to the different layers, together, and also responsible for the drug release across the skin. There is a provisionary surrounding of the adhesive layer by a backing and liner.

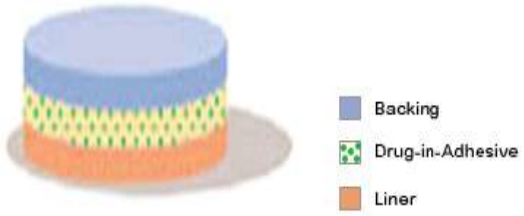

Fig.1: Single layer patch

Multi-Layer Drug In Adhesive: This form is similar to the single layer as well but includes a single layer. A layer of immediate drug release and other layers would be along with the adhesive sheet, controlled release. The release of the drug is the function of the adhesive sheet. This patch also has a temporary liner layer and permanent backing.

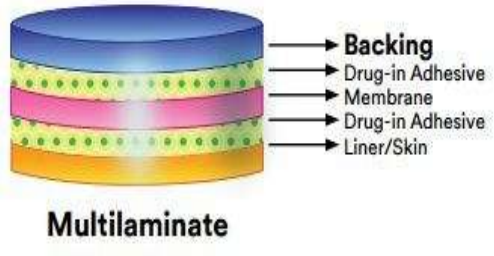

Fig. 2: Multi-layer patch

Vapor patch: The role of the adhesive layer in this form of patch is not only serves to adhere together the different layer, but also assist as a vapor release. The vapor patch are new to the market, often used in the release of essential oils congestion, decongestion. Other kinds of vapor patches are various often present in the market and used to boost the sleep efficiency and decrease the smoking of cigarettes situations.

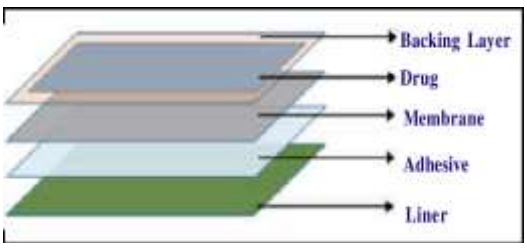

Fig. 3: Vapor patch

Reservoir system: In this device, between an impermeable backing layer and a rate control membrane, the drug reservoir is embedded. The drug is released only by the membrane that controls

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 864-869 www.ijprajournal.com ISSN: 2456-4494

the rate, which can be micro-porous or non-porous. The drug may be in the form of a solution, suspension, gel or distributed in a solid polymer matrix in the drug reservoir compartment. The hypoallergenic adhesive polymer can be used as a drug-compatible outer surface polymer membrane.

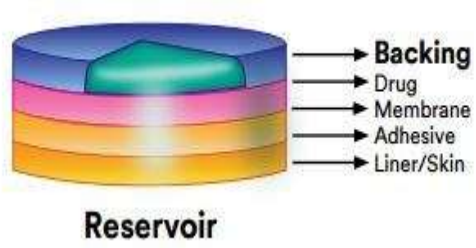

Fig. 4: Reservoir system

Structural components of transdermal patches:

Drug selection: The physicochemical properties of drug need to be considered in order to design transdermal patch. Hydrophobicity and ionization status are essential factors in drug selection as they influence skin penetration, evaluating drug solubility and diffusivity through the stratum conium skin layer. The melting point, aqueous solubility, partition coefficient(log p) , molecular size and molecular weight , dose concentration and saturation, permeability , absorbability and diffusivity through the stratum conium of human skin are the physicochemical properties of the drug that have a direct effect on skin penetration. Lipophilic drug comprise most transdermal patches, i.e. MW=500,< 1000 Daltons, log P ranges from 1 to 3 and MP < 250 ºC above the lower Burner Cooper boundary. For instance, fentanyl is present in moderate MW (337 Da), low MP (83 °C), and moderate to high lipophilicity (log P = 1-3). Drugs with low dose capacity, short half-life, quick hydrolysis in acidic media and those subject to hepatic metabolism will avoid the established problem when administered via transdermal patches.

Polymer matrix:

The polymer regulates the drug release from the system:

- **Natural polymer:** Derivatives of cellulose, zinc, gelatin, gums and their derivatives, shellac, waxes, fats, natural starch, rubber, etc.
- **Synthetic elastomers**: Poly butadiene, rubber hydrin, poly siloxane, silicone rubber, nitrile, butyl rubber, acrylonitrile, rubber from styrene butadieine, neoprene etc.
- **Synthetic polymers**: Polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene, polyacrylate, polyamide, polyuera, polyvinylpyrrolidone, polymethylmethacrylate, epoxy etc.

Permeation enhancer:

These are compounds that enhance permeability of the skin by altering the skin as a barrier to a desired penetrates flux. These can be grouped easily under the following major headings.

Solvents:

These compounds improve penetration likely by swallowing the polar pathway and/or by fluidizing lipids.e.g.

Alcohols: methanol and ethanol;

Alkyl methyl sulfoxide: dimethyl sulfoxide, dimethyl sulfoxide,

Alkyl homolog's: diethyl acetamidemethylsulfoxide

Pyrrolidones: 2 pyrrolidone

Permeation enhancer mechanism:

- These are chemical compounds that improve stratum conium permeability in order to reach a
- Higher drug therapeutic level.
- Permeation enhancers communicate with structural elements of the proteins and lipids of the stratum conium.
- They modify stratum conium protein and lipid packaging, thus chemically altering the barrier structure, resulting in increased permeability.

Surfactants:

These compounds are suggested to increase the polar pathway and transportation, especially hydrophilic drugs. The potential of the surfactant is a feature of the polar head group to alter penetration and chain length for hydrocarbons.

Anionic surfactants, e.g. Sulphosuccinate dioctyl, sodium lauryl sulfate

Nonionic surfactants, e.g.pluronicF127, pluronic F68 , etc.

Other Excipient:

Adhesives:

The fastening to the skin of all transdermal devices has done so far Using a pressure-sensitive adhesive that can be used for a long time, Positioned on the device's face or on the device's back and Peripheral stretching. Both adhesive systems should meet the requirements of following criteria

- It should be easy to adhere aggressively to the skin and removed easily

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 864-869 www.ijprajournal.com ISSN: 2456-4494

- No unwashable residue should be left on the skin
- The skin should not be irritated or sensitized.

Pressure sensitive adhesives:

Pressure sensitive adhesives are the material that stick to a substrate in the situation skin application of light forces and leaves no residue when evacuated. They form inter atoms and intermolecular attractive forces at the interface, provided that the cozy/intimate contact if formed. To acquire this level of content the material must be able to deform under slight pressure, offering ascend to the term pressure sensitive. Adhesive indicates a liquid like flow, bringing about wetting of the skin surface on the application of pressure, and when the pressure is expelled.

Types of pressure sensitive adhesive:

The different types of PSAs used in the delivery of transdermal drugs systems include, but are not limited to: polyisobutylenes, silicones, acrylates, & PSAs for hot melt.

- Polyisobutylene.
- Silicone
- Acrylates

Membrane backing:

Backing membranes are flexible and have a solid back membrane that attaches to the drug reservoir, prevents the dose from leaving the form of the drug until the end, and accepts printing. It is impermeable, because substances which, during use, protect the substance from the skin, e.g. Laminate metallic composite, absorbent pad with plastic backing, Occlusive base plate (aluminum foil), foam adhesive pad (polyurethane foam flexible) with occlusive base plate (aluminum foil disc).

Release liner:

With a sheet of protective film, the transdermal patch is secured. Immediately before the patch is applied to the skin, it is removed. This layer is part of the packaging of the main layers. It may be due to the liner's close touch with the form of dose. They also comply with all requirements relating to the inertness of the delivery system components and penetration properties. To create a release liner, fluoropolymers, fluoroolefin-based polymers, and linear fluoroacrylates are widely used.

Anatomy and physiology of skin:

The skin is the largest organ in the body, according for around 15% of the total adult body weight. The skin is continuous, through the mucous membranes which cover the surface of the body. The structure of the skin is made up of a complex network that acts as the body initial barrier against bacterial, UV light and chemical and mechanical injury. It also controls temperature and the amount of water released to the atmosphere.

Skin is one of the most readily accessible organs of the human body. There are two kind of human skin: one that is hair-less such as soles of foot and palms of hand, and the other kind which bears hair and sebaceous glands such as arms and face.

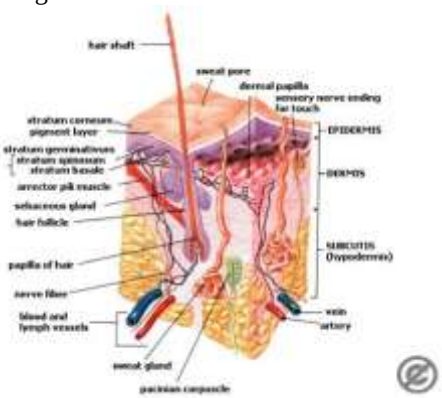

Fig.5: Anatomy of skin

Taxonomical classification:

The skin is divided taxonomically into three scales namely micro scale, meso scale and macro scale. The components of cell and layers of skin constitute the microscales they can only be seen under the micro scope and cannot be differentiated or identified with human eye. The meso scale comprises of skin features hair, freckles, moles, scale, comprises of the skin features, hair ,freckles, moles pores, skin surface and wrinkles as they can be seen with the naked eye and more clearly under the micro-scale if necessary. The macro scale compresses of body regions and body part. The skin morphology and appearance appears different at different part of the body.

Histological classification:

The skin is divided histological into the epidermis the dermis and the hypodermis which collectively forms a cover against external agent and loss of water from the body.

Skin layers:

Epidermis: The epidermis is the outermost layer of the skin. It is made up of multiple different layers that may change slightly depending on the location of the body. The layers of the epidermis include the basal stratum (the deepest component of the epidermis), the spinosum stratum, the granulosum

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 3 May-June 2022, pp: 864-869 www.ijprajournal.com ISSN: 2456-4494

stratum, the lucidum stratum and the coneum stratum (the most superficial portion of the epidermis). The main cell types exist in the epidermis keratinocytes, melanocytes, Markel cell and langerhans cells.

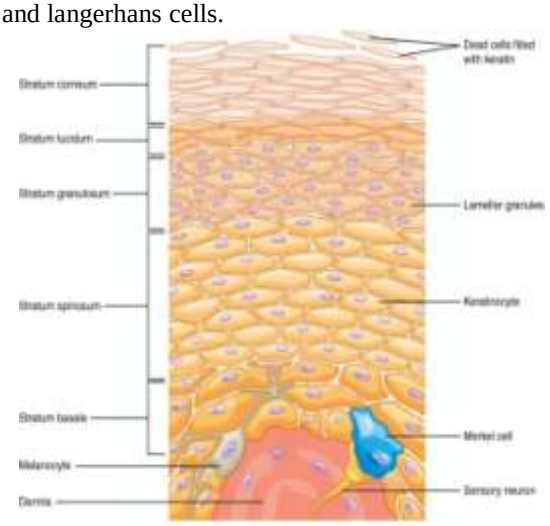

Fig 6: Structure of epidermis

There are four major cell types in the epidermis:

- Keratinocytes(skin cells)
- Melanocytes(pigment producing cell)
- Cell langerhans(immune cell)
- Markel cell

Dermis: As distinct from the epidermis (epi means "upon" or "over") and hypodermis (hypo means "below"), the dermis may be considered the "core" of the integumentary system (derma means "skin"). It includes vessels of the blood and lymph, nerves, and other structures such as follicles of the hair and sweat glands. Most of the dermis consists of thick irregular connective tissue, divided into two layers: the papillary and reticular layers. Numerous elastin and collage nous fibers are interwoven within these layers, formed by fibroblast.

Hypodermis:

Subcutis consists of loose connective tissue and fat in the abdominal parts that reaches up to 3 cm. Dermis has unique corpuscular receptors that allow Meissen's corpuscles and pacinian corpuscles, respectively, to feel touch and vibration. Both skin nerves in the dermis have an individual cell body that ends up in the free sensory nerve to sense temperature and itching on the surface of the skin. The dermal layer's autonomic nervous system impacts adrenergic fibers on the hair root muscles, blood vessels, and apocrine glands, while cholinergic fibers innervate eccrine sweat glands. The endocrine system controls the sebaceous glands and are not innervated by autonomic fibers .The plexus is formed by branches of the papillary and reticular dermal borders.

Approaches used in transdermal patch:

- Membrane moderate system
- Adhesive diffusion control system
- Matrix dispersion
- Micro reservoir system.

Recent advances in the field of transdermal patches:

- Patch technology for protein delivery.
- Pain-free diabetic monitoring using transdermal patches.
- Testosterone transdermal patch system in young women with spontaneous premature ovarian failure.
- Transdermal patch of oxybutynin used in overactive bladder.
- Nanotechnology gaining hold.
- Pain relief.
- Molecular absorption enhancement technology.

II. CONCLUSION:

The transdermal drug delivery system is most widely used routes of drug administration directly into the bloodstream without any pain; we can overcome the challenges associated with current drug delivery by formulating the drug as transdermal patches.

Transdermal drug delivery overcomes the issues associated with the drug having biological short half life and fluctuation in plasma concentration upon oral administration. Transdermal delivery system can defeat specific hurdles associated with conventional method of delivery e.g. drug that experience fractional or complete degradation before reaching,, the site of action could be effectively delivered with improved bioavailability by utilizing transdermal drug delivery system. It has great potential being able to use for both hydrophobic and hydrophilic active substance into promising deliverable drug. In this article provide all valuable information regarding the transdermal drug delivery system.

REFERENCES:

[1]. J. Ashok kumar, N. p., S.Lakshmana prabu, V. Gopal, (2010). Transdermal Drug Delivery System: An Overview. Int. J Pharm Sci Rev Res, **3**; 49-54.

[2]. Alkilani A., McCrudden M., Donnelly R., (2015). Transdermal drug delivery: innovative pharmaceutical developments based on disruption of barrier properties of the stratum corneum .MDPI, **7**, 438-470.
[3]. Jain, N.K., (1997). Controlled and novel drug delivery.CBS publisher and distributor;100- 130.
[4]. Cherukuri S., Batchu R., (2018). Formulation and evaluation of transdermal patch of topirate .International journal of pharmaceutical investigation, **7(1)**; 10-17.
[5]. Patel R.P., Patel G., (2009). Formulation and evaluation of transdermal patch of Acelofenac. International journal of drug deliver. **1**; 41-51.
[6]. Al Hanbali O.A., Khan H.M.S., Sarfraz, M.; Arafat, M.; Ijaz, S.; Hameed, A., (2019). Transdermal patches: Design and Current approaches to painless drug delivery. Acta Pharm. **69 (2)**; 197-215.
[7]. Lobo S., Sachdeva S., Goswami T. (2016). Role of pressure-sensitive adhesives in transdermal drug delivery systems. Ther.deliv. **7 (1)**;33-48.
[8]. Paul A. J. ,Kolarsick BS, Maria Ann Kolarsick,(2009). Anatomy and Physiology of the Skin, feature article, Oncology Nursing Society,**10**;203- 211.
[9]. Boulant J. A. (2000).Role of the preoptic-anterior hypothalamus in thermoregulation and fever. Clinical Infectious Diseases, **31(Suppl. 5)**;S157-S161.
[10]. CaputoR., Peluchetti D., (1977). The junctions of normal human epidermis: A freeze-fracture study. Journal of Ultra structure Research, **61(1)**;44-61.
[11]. Nafisi S., Maibach H.I., (2018). Skin penetration of nanoparticles. In Emerging Nanotechnologies in Immunology, Shegokar, R.; Souto, E. B., Eds. Elsevier: Boston; 47-88.
[12]. Ahmed N., Karki R.,Charde M., Charde B.,Gandhare,R. Road(2011). Transdermal Drug Delivery Systems: An Overview. International Journal Of Biomedical And Advance Research, **02(01)**; 38-56
[13]. H. A. E. Benson (2005). Transdermal Drug Delivery: Penetration Enhancement Techniques. Current Drug Delivery, **2(1)**; 48-56.