A REVIEW OF, EVALUATION AND EFFICACY OF TRANSDERMAL PATCH OF DICLOFENAC

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ABSTRACT :

The current research aims to formulate and evaluated medicated transdermal patches containing an diclofenac drug. A good penetration enhancer would improve drug delivery from various polymer based transdermal patches. Transdermal drug delivery influence consumer acceptance and marked increase in bioavailability of some drugs which undergoes hepatic first pass metabolism. it consists polymer and plasticizer, transdermal patches have different properties and different drug release. This study is on the basis of evaluate the amount to be needed for fabrication of DICLOFENAC transdermal patch. The field of transdermal drug delivery, aimed at developing safe and efficacious means of delivering medications across the skin. Transdermal patches are a non-invasive method of drug administration. It is an adhesive patch designed to deliver a specific dose of medication through the skin and into the bloodstream DICLOFENAC is a nonsteroidal anti – inflammatory drug that effectively manages pain, post – extraction pain is commonly treated with non-steroidal anti-inflammatory drugs. All prepared formulations were tested for weight variation, thickness, drug content, moisture content. Topical administration of therapeutic agents offers many advantages over conventional oral and invasive methods of drug delivery.

Keywords *: transdermal patch , diclofenac , topical medical patch, PVP k 30*

Introduction

transdermal drug delivery system are specific dosage forms which delivered the drug through a skin in predetermined and controlled rate. Transdermal drug delivery systems involved the topically administered medication in self-contained, discrete dosage forms of patches, which on application to the skin delivery the drug into bloodstream through skin portal at a predetermined controlled rate over a prolonged period of time. Transdermal drug delivery influence consumer acceptance and marked increase in bioavailability of some drugs which undergoes hepatic first-pass metabolism.

- **Transdermal patch of diclofenac :**

A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream often, this promotes healing to an injured area of body.

Diclofenac is non-steroidal anti-inflammatory agent, widely used in musculoskeletal disorders, arthritis, toothache, etc. ., for symptomatic relief of pain and inflammation.

History

Food and Drug administration in DECEMBER 2020 Nawazish et al. world journal of pharmacy and pharmaceutical sciences 1979 containing scopolamine for treating motion sickness (segal 2007).

The highest selling transdermal patch in the United States was the nicotine patch The first commercially available prescription

patch was approved by the U.S. which releases nicotine to help with cessation of tobacco smoking. The first commercially available vapour patch to reduce smoking was approved in Europe in 2007.

Early Devlopment

The first transdermal patch was developed in the 1970s . Sherman and dale Wurster are credited with the early stages of transdermal patch delivery in 1961

PATHOPHYSIOLOGY

Diclofenac is a nonsteroidal anti-inflammatory drug that reduces pain by blocking the body production of certain chemicals , which are applied topically ,can be administered systemically in low concentrations. It is possible to reduce the strength of action and the ensuring side effects associated with oral delivery.

Diclofenac is a NSAIDs that inhibits both cyclooxygenase (COX)-1 And cyclooxygenase (COX)-2 enzymes.

NSAIDS inhibits the synthesis of prostanoids and thromboxane by binding to COX isozymes. PGE2 is the dominant prostanoid produced in inflammation, and inhibiting its synthesis is by NSAIDS is believed to be the primary mechanism of these agents potent analgesic and anti-inflammatory properties .

- **Permeation through Dermis**

Skin :

skin is the largest organ of human body.

Transdermal delivery system are non-invasive systems for delivering medications into the dermis.

Skin is very effective as a selective penetration barrier, the epidermis provides the major control element for drug penetration. the drug initially penetrates through the stratum corneum and then passes through the deeper epidermis and dermis without drug accumulation in the dermal layer.

When drug reaches the dermal layer it becomes available for systemic absorption via the dermal microcirculation.

- **Skin has mainly: 3 layers**

1. **Epidermis**
2. **Dermis**
3. **Hypodermis**

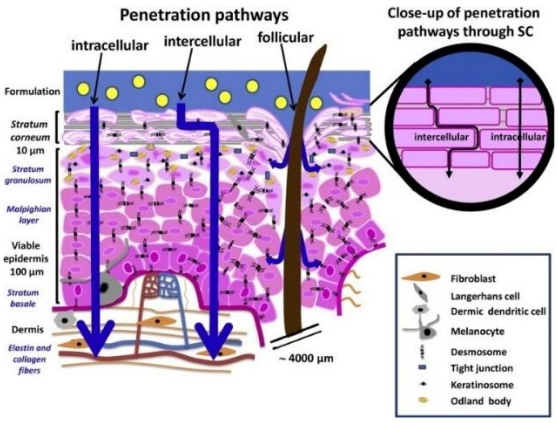


Fig ; Structure of skin

1 . Epidermis

The epidermis is skins outermost layer and having 150 micrometer thickness.

The skin can be considered to have four distinct layers of tissues including non-viable epidermis (stratum corneum), viable epidermis, viable dermis and hypodermis (subcutaneous connective tissue). The epidermis is relatively thin, tough outer layer of the skin The epidermis has keratinocytes, and other cells of the of the epidermis layer including melanocytes, langerhance and merkel cell. The stratum corneum is the most superficial layer of the epidermis.

It composes with 5 layers

1. **stratum corneum** : It consist of 10 to 25 layers of flattened dead keratinocytes, which makes water repellent.
2. **Stratum Lucium** : It is a thin layer , clear layer of dead skin cells in the epidermis named for its translucent appearance under a microscope.
3. **Stratum Granulosum**: It consist of 3 to 5 layers and under goes apotosis . it contains granules known as keratohyalin.
4. **Stratum Spinosum**: It contains 8 to 10 layers of cells and it is closely arranged.
5. **Stratum Basale**: It consist of single layer of cubical or columnar keratinocytes.

2 . Dermis

It is composed of strong connective tissue containing collagen (70%) and elastic fibers give strength and elasticity to the skin. Hence it can easily stretch and recoil easily.

The nerves glands, blood vessels and hair follicles are embedded in this layer. (9)blood vessels found in the dermis provide nutrients for both the dermis and epidermis . nerves, macrophages and lymphatic vessels are also present in the dermis layer.

3 . Hypodermis

adipose tissue. This helps to insulate the body by monitoring heat gain and heat loss. it is the deepest layer of the skin and consist of a network of fat cell. Hypodermis is tissue made up of loose connective tissue, including The major functions of the hypodermis are protection against physical shock, heat insulation and support and conductance of the vascular and neural signals of the skin . approximately 50% of the body fat with the other predominant cells of the hypodermis consisting of fibroblasts and macrophages.

***Permeation of drug through skin:**

Drug molecules permeate through skin surface by the different potential pathways including through the sweat ducts through the hair follicles and sebaceous glands or directly across the stratum corneum.

↓Two possible routes of drug penetration across the intact skin

1 **Transepidermal** 2 **Transappendegeal**

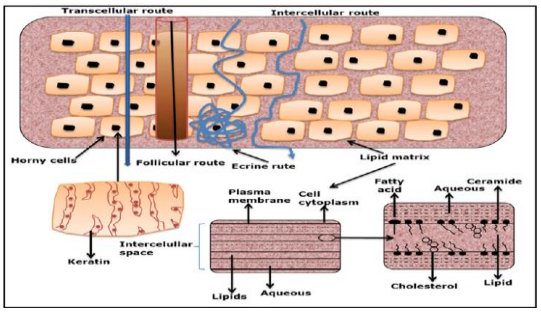


Fig : Permeation of drug through skin

***Key factors affecting permeation :**

1 . physiochemical properties of the drug :

Molecular weight : smaller molecules typically penetrates more easily.

Lipophilicity : lipid -soluble drugs tend to permeate better through the lipid – rich stratum corneum

Polarity : non- polar compounds generally have better permeation compared to highly polar ones.

2 . formulation:

Vehicle: the choice of formulation affects drug solubility and stability

Enhancers: chemical permeation enhancers can disrupt the stratum corneum, increasing drug absorption .

3 . skin condition:

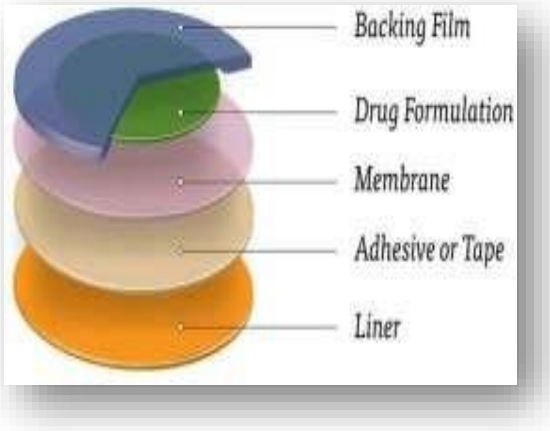
hydration: well hydrated skin can enhances permeation.

. duration of application: prolonged contact can improve drug uptake.

. application site: different areas of the body hsve different permeability profiles .

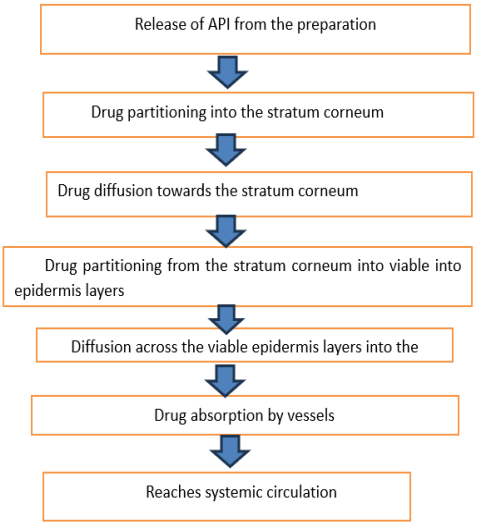
Application of permeation:

Transdermal delivery systems are used for various therapeutic agents, including pain relievers , hormones , ets.



Permeation of drug through skin:

- **Flow chart:**



❖ Components of TDS :

Fig No 3 :Components Of Transdermal Patch

- **Components of TDS :**

Drug: For developing a TDDS, the drug should be chosen with great care,
The drug should be potent, having short half-life and be non-irritancy.
The drug should have molecular weight less than 1000 daltons.
The drug should have low melting point.
The drug should have affinity for both lipophilic and hydrophilic phases.

1. **Polymer matrix:**

Polymer controls the release of the drug from the device.
Polymer should have biocompatible and chemically compatible with drug and other components of the system.

1. Natural polymers: cellulose derivatives, waxes , gums , natural rubber, starch , etc.
2. Synthetic elastomers: polybutadine , hydrin rubber , silicone , styrene , etc.

3. Synthetic polymer: polyvinyl alcohol , PVC , polyethylene, polyacrylate , epoxy etc.

2 . Permeation enhancers:

These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrate.

These may conveniently be classified under the following main hedings :

a) **Solvents**: these compounds increases penetration posiibly by swallowing the polar pathway or fluidizing lipids.
Example; water alcohols – methanol, ethanol, pyrrolidone

b) surfactant: these compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs.

The ability of a surfactant to the alter penetration is function of the polar head group and the hydrocarbon chain length.

1 **Anionic surfactant**: e.g. . dioctyl sulphosuccinate, sodium lauryl sulphate
2 **Non ionic surfactant**: e.g . pluronic F 127, pluronicF68, etc .
3 **Bile salts**: e.g . sodium mstaurocholate , sodium deoxycholate , sodium tauroglycocholate .

c)Miscellaneous chemicals : These include urea, a hydrating and keratolytic agent; N, Ndimethyl-m-toluamide; calcium thioglycolate; anticholinergic agents.

Some potential permeation enhancers have recently been described but the available data on their effectiveness sparse.

These include eucalyptol, di-o-methyl-ß-cyclodextrin and soyabean casein.

4. other excipients :

a) adhesives: the fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face of the devices or in the back of the devices and extending peripherally.

both adhesive systems should fulfill the following criteria :

4 Should adhere to the skin aggressively, should be easily removed.
5 Should not leave an unwashable residue on the skin .
6 Should not irritate or sensitize the skin
7 Permeation of drug should not be affected.
8 The delivery of simple or blended permeation enhancers should not be affected.

b) **backing membrane**: backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, band accept printing.

It is impermeable substances that protects the product during use on the skin.

e.g plastic laminate, aluminum foil, adhesive foam pad with occlusive base plate (aluminium foil disc) etc.

Types of transdermal drug delivery system:

1 . **Single – layer drug in adhesive:** single layer drug in adhesive the single layer drug in adhesive system is characterized by the inclusion of the drug directly within the skin contacting adhesive. In this transdermal system design, the adhesive not only serves to affix the system to the skin, but also serves as the formulation foundation , containing the drug and all the excipients under a single backing film. The rate of release of drug from this type of system is dependent on the diffusion across the skin

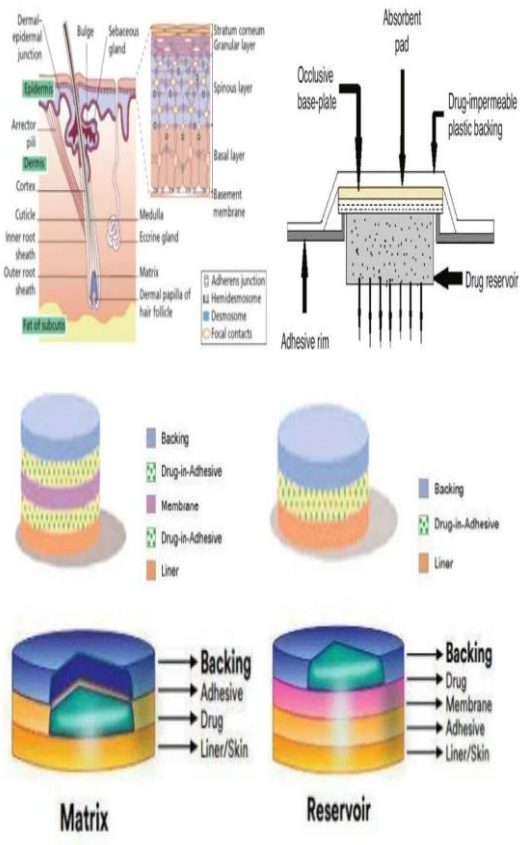
.

2 . **Multi- layer drug in adhesive**: The multi-layer drug in adhesive is similar to the single layer drug in adhesive in that the drug is incorporated directly into the adhesive. However, the multilayer encompasses either the addition of a membrane between two distinct drug in adhesive layers or the addition of multiple drug in adhesive layers under a single backing film.

3 . **Drug reservoir in adhesive**: The reservoir transdermal system design is characterized by the inclusion of a liquid compartment containing a drug solution or suspension separated from the release liner by a semipermeable membrane and adhesive. The adhesive component of the product responsible for skin adhesion can either be incorporated as a continuous layer between the membrane and the release liner or in a concentric configuration around the membrane.

4 **Drug matrix in adhesive**: The matrix system design is characterized by the inclusion of a semisolid matrix containing a drug solution or suspension which is in direct contact with the release liner. The component responsible for skin adhesion isincorporated in an overlay and forms a concentric configuration around the semisolid matrix.

- **Schematic representation of types of TDDS**



- **Fig: schematic representation of types of TDDS**
- **Advantages of transdermal patches:**

Avoidance of first pass metabolism Avoidance of Gastrointestinal incompatibility.

Avoiding in drug fluctuation levels.

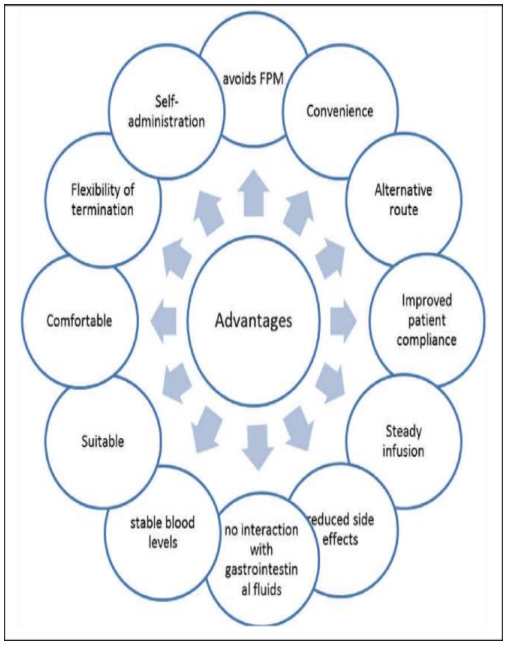
Provide suitability for self-administration.

Transdermal patches are cost effective.

Minimizing undesirable side effects.

It is a convenience

It reduced side effects.



Benefits of transdermal patches:

Prolnge duration of action.

Drug molecule must be POTENT

Improved bioavailability

Reduced systemic side effects.

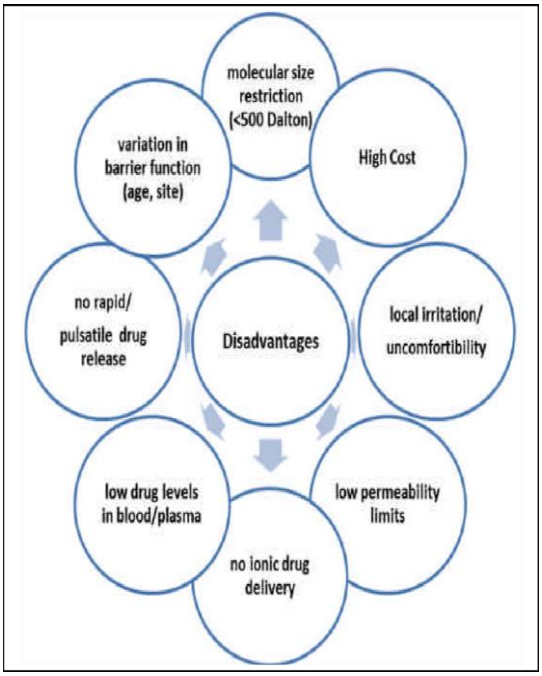
Disadvantages of transdermal patches:

TDDS cannot deliver ionic drugs.

If cannot achieve high drug levels in blood.

It may cause allergic reactions.

Possibility of local irritation at site of application.



Efficacy of transdermal patch of diclofenac:

Transdermal diclofenac patches have demonstrated efficacy in managing pain and inflammation with a favorable safety profile. They provide effective localized treatment , making them a suitable option for many patients , especially those who prefer non oral routes of administration

Clinical application:

Diclofenac transdermal patch have been effectively used In various clinical settings:

- Postoperative pain management
- Orthodontic extraction
- Third molar surgeries
- Osteoarthritis treatment

Transdermal patch of diclofenac:

Fig :Transdermal patch

Techniqeus for enhancement of skin permeation :

*** .transdermal drug delivery technologies** :

A . active methods :

1 . Thermal ablation :

Laser radiation , radiofrequency

2 . Electrical:

Iontophoresis , electroprporation

3 . mechanical approaches:

Microneedle

4 . physical approaches:

Jet injector , ultrasound

B . passive methods:

1 . vesicles

2 . chemical enhancers

Drug profile of diclofenac:

Class : Non steroidal anti-inflammatory drug (NSAID)

MOA: Diclofenac works by inhibiting cyclooxygenase enzyme , which are involved in the synthesis of prostaglandins. This results in reduced inflammation, pain and fever .

Function of diclofenac : diclofenac transdermal patch topical administered to relief pain .

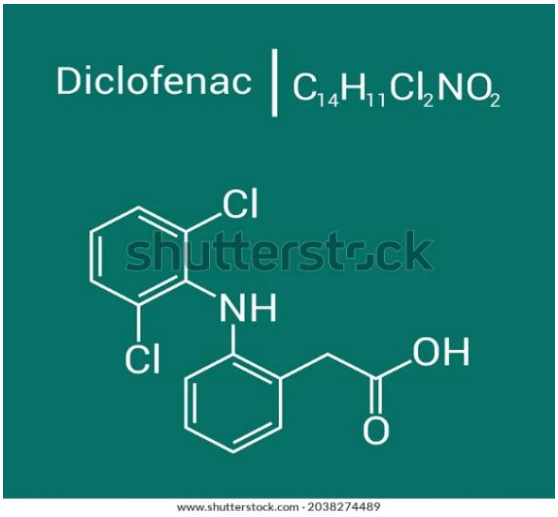


Fig : Chemical structure of diclofenac

CONCLUSION :

our study concludes that transdermal Diclofenac in patients with chronic musculoskeletal pain. Further study of longer duration is needed to evaluate the safety of transdermal Diclofenac patch. the analgesic efficacy of Diclofenac Transdermal patches is promising. Due to improved delivery and a more comprehensive selection of painkillers, this method is expected to become more popular and widely used there are many enhancement strategies that can be applied for improving transdermal delivery system. transdermal patch technology is a valuable drug delivery method with many advantages over other delivery routes.

Reference:

1. *Schnitzer TJ. Update on guidelines for the treatment of chronic musculoskeletal pain. ClinRheumatol 2006;25 Suppl 1:S22-9.*
2. *Anselmo, A.C.; Mitragotri, S. An Overview of Clinical and Commercial Impact of Drug Delivery Systems. J. Control. Release 2014, 190, 15-28.*
3. *Md. IntakhabAlamı, NawazishAlam*2, Vikramjit Singh2, Md. Sarfaraz Alam1, Md. SajidAlil, TariqueAnwerl, Mohammed M. Safhil TYPE, PREPARATION AND EVALUATION OF TRANSDERMAL PATCH: A REVIEW.2013. Volume 2, Issue 4. 2199-2233. ISSN 2278 - 4357*
4. *Himanshitanwar R.Transdermal Drug Delivery System, Advance Development AndEvaluation-A Review. Int J Pharma SciRes.2016:8(2):385-400. Doi:10.13040/IJPSR.0975- 8232.8(2).385-00.*
5. *Sachan R, Bajpai M. Transdermal drug delivery system: a review. Int J Res Dev Pharm. 2013;3(1):2278-90. doi:10.13040/LJPSR.0975 8232.7(6).2274-90.*
6. *Naik, A.; Kalia, Y.N.; Guy. R.H. Transdermal Drug Delivery: Overcoming the skin's BarrierFunction. Pharm. Sci. Technol. Today 2000, 3, 318-326.*
7. *Zorec, B.; Préat, V.; Miklavčič, D.; Pavšelj, N. Active Enhancement Methods for Intra- andTransdermal Drug Delivery: A Review. ZdravniškiVestnik 2013, 82, 339-356. (In Slovenian)*
8. *Chien, Y.W, Liu, J.C. Transdermal drug delivery systems. J. Biomater. Appl. 1986, 7, 183-206. CrossRef]*
9. *Lasagna, L.; Greenblatt, D.J. More than skin deep: Transdermal drug-delivery systems, N. Engl. J. Med. 1986, 314, 1638-1639, [CossRef]*
10. *Berner, B.; John, V.A. Pharmacokinetic characterisation of transdermal delivery systems. Clin. Pharmacokinet. 1994, 26, 121-134[CrossRef]*
11. *Kumar, L.; Verma, S.; Singh, M.; Chalotra, T.; Utreja, P. Advanced Drug Delivery Systems for Transdermal Delivery of Non-Steroidal Anti-Inflammatory Drugs: A Review. Curr. Drug Delin 2018, 15, 1087-1099, [Cross Ref] [PubMed]*
12. *Li, W.Z., Hun, M.R.; Zhou, JP, Zhou, Y.Q; Hao, B.H.; Liu, T., Zhang, Y. Super-short solid silicon microneedles for transdermal drug delivery applications. Int. J. Pharm. 2010, 389, 122-129. [CrossRef]*
13. *Kolarsick PAJ, Kolarsick MA, Goodwin C. Anatomy and physiology of the skin. OncolNurs Soc. 2011;3:203-13.*
14. *Boer M, Duchnik E, Maleszka R, Marchlewicz M. Structural and biophysical characteristics of human skin in maintaining proper epidermal barrier function. PostepDermatolAlergol. 2016;33:1-5.*
15. *Böhling A, Bielfeldt S, Himmelmann A, Keskin M, Wilhelm KP. Comparison of the stratum corneum thickness measured in vivo with confocal Raman spectroscopy and confocal reflecte microscopy. Ski Res Technol. 2014;20:50-7.*