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Review Article

Penetration Enhancer: A Novel Stratagem for Transdermal Patches of Diclofenac Sodium for Immediate Post Analgesia

Anup Pramanik*, Dipayan Purakayastha, Tuman P. Rai, Madhvi Ghadge, Shiv Garg

Dept. of Pharmaceutical Sciences, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302039, Rajasthan, India

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ABSTRACT

The aim of recent work was to developed transdermal patch/film by the uses of two polymers of Polyvinylpyrrolidone (PVC) and methylcellulose (MC) with combination of the drug diclofenac sodium. The transdermal patches were prepared and evaluated by various physical as well as mechanical techniques. The objective of the patch was the accomplishment that the drug combined methods for the delivery of drug at a controlled release through the skin to body mechanism and shown a therapeutically effective drug level for a long time duration by transdermal patch. The release of the drug was found to follow first order rate kinetic effect.

Key words: Skin, Transdermal, Permeation pathways, Evaluation method, Future keystone.

Address for Correspondence: Anup Pramanik, Dept. of Pharmaceutical Sciences, Maharishi Arvind College of Pharmacy, Ambabari, Jaipur-302039, Rajasthan, India; E-mail: gargshiv81@yahoo.co.in

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INTRODUCTION

The word 'Transdermal' is made upon by two combination of words, one is transfer & another one dermal layer in our skin that means transfer the drug molecules in our body's part through the dermal layer. Our skin has attractive much attention for transfer the systemically drugs via this route. Many types of advantages present with transdermal drug delivery are well. Transdermal drug delivery system are explain as self contained & predetermined amount of drug combination forms which are applied to the skin, deliver the drug, at controlled rate of drug release to the systemic circulation. Last few years, this drug delivery formulation has been changing into stylish or modernise looking in cosmetic products which they are provide for elicit pharmacological effect via drug molecule. It's not only enhances the performance of the drug molecules through the therapeutic effect and safety but also increase patient willingness. Most advantages of these drug delivery system are limitation of hepatic first pass metabolism, prolonged of action, therapeutic effectiveness of potent drugs. Its short half-life provided drug's more effective value.

Now a-days the pharmaceutical industries are make various type of dosage forms which are applied through the skin for treatment of various disease and identified these diseases symptoms. Delivering medicines through the skin is more efficient and greater bioavailability choice of route because of an oral route causes some problems in internal body mechanism like first pass metabolism, poor bioavailability, and tendency which produce high and low rapid blood level.

The skin is the largest organ in the body, it protects from many more problems like the influx of toxins and efflux of water and penetration of foreign molecules. Human skin mostly consists of three layers:
(i) The epidermis
(ii) The dermis and
(iii) The hypodermis

The diclofenac sodium is potent non-steroidal anti-inflammatory drugs (NSAIDs). The primary mechanism of diclofenac sodium are anti-inflammatory, antipyretic and analgesic action is thought to be inhibition of prostaglandin synthesis by inhibition of the transiently expressed prostaglandin-endoperoxide synthase-2 (PGES-2) also known as Cycloxygenase-2 (COX-2). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis. Sometimes Diclofenac sodium inhibits the lipoxygenase pathways, thus reducing formation of the leukotrienes.

Advantages:

1. Transdermal drug delivery system avoidance of first pass metabolism of drugs.
2. It reduced plasma concentration levels of drugs.
3. This is mostly work for reduction of fluctuations in plasma levels of drugs.
4. Reduction of dosing frequency an enhancement of patient compliance.
5. Transdermal medications deliver a steady infusion of a drug over an extended period of time.
6. This route of drug delivery system increase bioavailability.
7. It eliminates gastrointestinal side effects.
8. TDDS potential for home administration.
9. Easy to modulate the drug release rate.

Limitations:

1. Transdermal drug delivery system cannot carry ionic drug molecules.
2. It cannot make large number of molecular size drugs.
3. Sometimes it causes irritation to skin.
4. This type of drug delivery system cannot apply in tinnitus fashion.

Drug Penetration Pathways

The permeation of the drugs through the skin by diffusion method in epidermis layer and appendages of skin. Drug can be penetrated by three pathways such as transcellular route, paracellular lipid route and transappendgeal route.

- Transcellular Route: In this route mostly passes the moiety through both keratinocytes and lipids.
- Paracellular Route: This is the most common penetration pathway of drug molecules. In this pathway, drug remains in lipid moiety and stay around keratin.
- Transappendgeal Route: This route makes continues channel for drug permeation but it hindered easily due to presence of hair follicles and sweat ducts.

Ways to Enhance skin penetration

There are various types of route to differentiate and classify skin penetration enhancers. This classification divides penetration enhancers into three main categories, write below points:

i. Solvents are play a vital role for enhancing the penetration through both polar and non-polar pathways like N-methyl formamide, 2-pyrrolidone etc.
ii. The polar route affect shown for enhancer that preferentially like propylene glycol in combination with decylmethysulfoxide.

iii. Lastly, the non-polar routes are modify for enhances the skin permeation like propylene glycol and oleic acid.

Physical Penetration Enhancers

- **Electroporation:** It is a method of enhancing diffusion across biological barriers of body. It involves the application of high-voltage pulses to induce skin perturbation. The combination of high voltages and short treatment durations are most frequent affect shown in body mechanism and other electrical parameters that affect delivery includes pulse properties such as waveform, rate and number of the frequency show of the drug molecules.
- **Iontophoresis:** Iontrophoresis method involves enhancing the permeation of a topically applied therapeutic agent by the application of low-level electric current. Increases the drug permeation as a result of this methodology can be attributed to either one or a combination of electrorepulsion, electroosmosis and electroperturbation mechanism.
- **Ultrasound:** It involves the use of ultrasonic energy to increases the transdermal delivery of solutes either continuously or through pre-treatment. The expected mechanism behind the increase in skin permeability is attributed to the formation of gaseous cavities within the intercellular lipids on exposure to ultrasound.

Chemical Penetration Enhancers

The report of articles describing various compositions which may contain materials particles increases the penetration activity. Various type of mechanism process are used for enhancing the penetration by these properties. They are generally classified on their chemical structure and act on skin by variety of mechanisms. These mechanisms are mostly depending on their physicochemical properties, biological effects of body mechanism and used chemicals belonging to the same group may have different mechanism.

Chemical Name	Enhancers
Amides	Azone
Esters	Ethyl acetate, Isopropyl myristate
Fatty acids	Lauric acid, Palmitic acid
Sulfoxides	Dimethyl sulfoxide
Surfactants	Anionic surfactants, Span 80
Terpenes	Cineole, D-Limonene, Linalool

Table 1: Examples of Penetration enhancer

Factors affecting Skin Penetration

The subcutaneous is a heterogenous structure of skin. Microscopically, the upper cells of the epidermis, the corneocytes are arranged in pillars to form bunch. Like that a composition favours the absorption of certain lipid-soluble compounds by the skin. Scientist has developed some model for simple diffusion to explain the flux of compounds through subcutaneous lipid domains. This module is assuming that interaction between a given compound and the skin is physicochemical in nature, with the multilayer structures of the skin. The majority of molecules that cross the epidermis will permeate between the skin cells. Therefore, the major pathways of the compound are highly dependent upon its partition coefficient. Hydrophilic compounds may preferably partition into the intracellular domain, while lipophilic one may be cross the subcutaneous through the intercellular route.

Mind it before applying transdermal patch

- Before applied this drug dosage form should be properly cleaned of the skin.
- Old patch should be removed before applying new patch.
- If applying area of patient is small then don't cut the patch because it destroys form of drug properties.
- The patch should be placed on accurate area.

MATERIALS AND METHODS

Materials: All the chemical products and procedure were used as standard pharmaceutical grade. Diclofenac sodium was procedure as a gift sample from (Lark Laboratories India Ltd., New Delhi), Polyvinylpyrrolidone (PVP) (Alpha Chemika, Mumbai, India), Polyvinyl alcohol (PVA) (viscosity of 4% aquous solution), Chloroform (in college), Dibutylphthalate (in college), Methanol (college level), tween 80 and Methyl cellulose (MC) were got sufficient quantity. After taken these chemical products were used for further testing purposes.

Ingredients	Category
Diclofenac sodium	Drug
Polyvinyl pyrrolidone	Polymer
Polyvinyl alcohol	Polymer
Methyl cellulose	Polymer
Dibutyl phthalate	As a plasticizer

Table 2: List of Components

Methods

All of these chemical products were used on their particular chemically required bases. Diclofenac sodium was a raw drug form which used in particular quantity for prepare the patches. The lower part of the old was covered with aluminium foil paper. Required quantity of polyvinyl alcohol (PVA) was taken and its easily water soluble polymer. Then prepared a mixture with water and PVA by slow addition constantly stirring until it prepared a homogeneous mixture. The aluminium foil backing membrane was cast by pouring with 2% w/v polyvinyl alcohol solution and 4% of w/v polyvinyl alcohol solution into the glass molds drying at 80-100˚C for 24 hours. After drying the above two combinations of 4% PVP was screened and achieved and used for backing membrane preparation.

Transdermal patches of diclofenac sodium were prepared using PVP and ethyl cellulose (EC) through the solvent evaporation technique in glass molds.

Rate controlling membrane

The transdermal patches formulation quantity shown above in table no.1 was prepared by solvent casting method. The polymers were dissolved in methanol at room temperature with continuous stirrer at slowly rpm initially and higher speed rpm later.

Evaluation and Characterization

The formulation of the transdermal patch has considerable influence on physical and chemical properties as well as the permeability of the drugs. Various type of evaluation methods were used for tested the patches such as thickness uniformity, percent flatness, percent elongation, tensile strength and modules of elasticity studied.

(i) Physical Appearance: All type of transdermal patches were visually checked for colour, shape-size, smoothness and flexibility.

(ii) Thickness of the patch: Measured the thickness of patch was many type of mechanical instruments like dial calliper, screw gauze etc. and write down the mean value.

(iii) Weight Uniformity: It was measured by the digital balance after dried patches and calculated the average value.

(iv) Folding endurance: It is mainly describe no. of times the patch folded at same place either to break the drug coated portion of the patch or to shown cracks on the outer part of patches. A patch was cut and repeatedly folded at same place and stop when it totally breaks into some parts. Then counted the number of folded times of the film which was folded at the same place before break and calculated the average value of folding endurance. This test also described the brittleness of any film after checked; more brittleness shown when less folding endurance indicates.

(v) Percentage moisture content: The prepared patches were weighed and kept in calcium chloride filled desiccators at room temperature for a day. After this time duration the patches were again weighed and determine the percentage content.

(vi) Percentage moisture uptake: As same as the above procedure of percentage moisture content in this here the patches were kept in a saturated solution of potassium chloride desiccators for a day at room temperature and maintain the 84% room humidity. After 24 hours the patches were again weighed and determine the percentage moisture uptake.

(vii) Tensile strength & Percentage Elongation: The patches were taken in a containers using required quantity of the solution and cut into small pieces. Then the pieces were fixed onto the tensile strength apparatus. Tensile strength was calculated by

Tensile strength Formula = [break force (1+ change in length)] / [(width × breadth) (initial length of the film)]

The percentage elongation was determine before the break point of the patch and put the value in below formula

Percentage Elongation = [(final length – initial length) / initial length] ×100

Future Keystone

A successful transdermal system requires good nature of the patch and function of the site of application. The real example of transdermal patch should be pharmacologically inert, non-toxic, non-irritant and non-allergic; it should have reversible action on skin without any problems. The safe and good effect show of the drug delivery is the ultimate vision for each and every current technology ever explored. A little examination has been done on penetration rates and amount of penetration on the skin in a particular time of duration.

DISCUSSION

Duration of post analgesia studies by using visual analogue scale (VAS). It is a method used to grade pain by self assessment. Control release of drug delivery system through the transdermal films are

used for wide range to developed many of difficulties associated for administration. This route drug delivery system are available various forms like polymer based gel, gel spray, pellets, nanoparticles, microparticles, patch etc. They are two-component semi-solid drug carriers that contain high levels of fluid and viscosity enhancing agents.

The drug, diclofenac sodium transdermal patches for postoperative shoulder pain was studies by Lennart Funk, Umaar Molajoa of Bridge Water Hospital, Manchester, United Kingdom. Shoulder surgeries can now be performed as daycare producers thanks to advancement in minimally invasive techniques and regional for anaesthesia.

This patch has proven to reduce pain and inflammation in direct treatment of acute and chronic inflammation conditions of our body. The release of the drug ingredients over 12-18 hours period with less systemic side effect than oral forms and better patient compliance and easy way applied process on site of action.

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