COMPOSITION AND ANALYZATION OF TRANSDERMAL DICLOFENAC SODIUM PATCHES

Abhilash Kutlehria[*1], Rittika Choudhary[1], Kapil Kumar Verma[2]

[*1]*Assistant Professor, Minerva College of Pharmacy, Indora, Himachal Pradesh, India*

[1] *B.Pharma Scholar, Minerva College of Pharmacy, Indora, Himachal Pradesh, India*

ABSTRACT

Transdermal patches are gaining prominence as an alternative to oral drug delivery, offering controlled release and improved patient compliance. This study focuses on the composition and analysis of transdermal patches containing Diclofenac Sodium, a non-steroidal anti-inflammatory drug (NSAID) used for pain and inflammation management. The patches were formulated using various polymers, including hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA), alongside plasticizers like glycerin and enhancers such as propylene glycol to ensure optimal drug release and skin permeability. The patches were prepared via solvent casting and characterized for their physicochemical properties, including thickness, weight uniformity, drug content, moisture content, and tensile strength. In vitro drug release studies were conducted using Franz diffusion cells, while Fourier-transform infrared spectroscopy (FTIR) was utilized to assess drug-polymer interactions. Results indicated that polymer composition significantly influenced the drug release profile, with an ideal balance between film flexibility and sustained drug release.

The study concluded that transdermal Diclofenac Sodium patches present a viable method for controlled drug delivery, offering consistent drug release over time with minimal side effects. The formulation and evaluation process underscores the importance of optimizing polymer types and concentrations for effective transdermal therapy.

Keywords : *Transdermal Patch, Diclofenac, Inflammation, Controlled release, Polymer, Sustained release drug*

INTRODUCTION

The largest organ in the human body is the skin. Since the oldest known clinical records of mankind, drugs have been used topically to address superficial problems, for transdermal organization of therapies to manage underlying disorders, and as cosmetics. For instance, the use of cures, salves, elixirs, and even fixes, consisting of plant, animal, or mineral concentrates, was well-known in ancient Egypt and Babylonian medicine at that time.

A transdermal patch is a sedative patch that can directly and at a prescribed rate transfer medications into the bloodstream via the skin's layers. In actuality, patches are the most useful organizational tactic. They don't hurt, and you can stop the treatment at any time or continue for a few days. They have several fasteners and are available in different sizes. Through dispersion mechanisms, the fix can introduce dynamic fixes into the fundamental flow when administered topically. High concentrations of dynamic chemicals that remain on the skin for a long time may be found in transdermal patches. The dynamite fix was one of the first transdermal patches developed in 1985.

A rate-controlling ethylene vinyl acetic acid derivation film is used in Storm and Berggren's repair. Some drugs are currently available as transdermal patches, such as nicotine, fentanyl, clonidine, scopolamine (hyoscine), and estradiol derived from norethisterone acetic acid. Depending on the medication's therapeutic classification, there may be differences in the site of use. For example, you can apply

estradiol around the middle and dynamite around the chest. In addition, the duration of medicine release varies according to usage, ranging from the shortest (up to nine hours) to the longest (up to nine days).

Transdermal fix generally refers to skin application that allows medical professionals to solid, undamaged skin, either for basic treatment or for restricted treatment of tissues beneath the skin. Compared to conventional measurement forms or controlled discharge oral frameworks, Transdermal Fix has several advantages. Transdermal fix avoids portion unloading, expands patient consistency, avoids first pass digestion, and provides stable blood levels. The major barrier to penetration over the skin, which is essentially connected with the outermost layer of the epidermis called the corneum layer, restricts the use of transdermal delivery to a wider range of drugs. Plan on skin can be divided into two kinds based on the activity's objective location.

Following medication absorption from the cutaneous microvascular organization, one exhibits basal activity while another exhibits localized effects in the skin. Transdermal medication delivery can closely mimic the slow intravenous mixture without the anticipated risks. It also offers the patient the additional benefit of allowing them to stop their medication treatment by simply stopping the fix when they want to, assuming poisoning occurs.

TRANSDERMAL PATCHES

A transdermal patch is used to penetrate the skin and enter the bloodstream to administer a prescribed dosage. The FDA approved transdermal patch products for the first time in 1981. Nowadays, transdermal administration systems including scopolamine (hyoscine) for motion sickness, nitroglycerin and clonidine for cardiovascular disease, fentanyl for persistent pain, and nicotine to help with quitting smoking are available. Transdermal delivery allows for controlled, continuous drug administration, prevents pulsed entry into systemic circulation, and allows continuous input of drugs with short biological half-lives. When comparing TDDS to oral and conventional injectable methods, there are a lot of advantages. It eases the burden that eating a lot imposes on the digestive system and liver. It lessens the detrimental pharmacological side effects caused by temporary overdose and increases patient compliance. It is especially helpful for patches that only require weekly application. A simple dosing plan like this encourages patients to follow their prescription regimen.

COMPONENTS OF TRANSDERMAL PATCHES

- **Polymer matrix**– It is the core of TDDS, which regulates the medication's release. Polymers ought to be non-toxic, non-reactive to chemicals, and inexpensive. They should also not break down during storage. For instance, gelatin, shellac, zinc, cellulose derivatives, waxes, and gums Neoprene, nitrile, acrylonitrile, silicon rubber, polybutadiene, hydrin rubber, polyisobutylene, polyethylene, polypropylene, polycrylate, and polyamide.
- **Drug**- For medications with the right physical chemistry and pharmacology, the transdermal route is a very alluring choice. Drugs with a short half-life, a small therapeutic window, or substantial first pass metabolism can all benefit greatly from transdermal patches.such as nitroglycerines, fenatyl, etc.
- **Permeation enhancers-** Boost the stratum corneum's permeability to achieve greater therapeutic medication concentrations. These come in three varieties: two component systems, lipophilic solvents, and surface active agents. For example: DMSO.
- **Adhesive-** Boost stratum corneum permeability to achieve greater therapeutic medication levels. Boost stratum corneum permeability to achieve greater therapeutic drug levels.
- **Backing laminates-** Should have low modulus or high flexibility. Eg-vinyl, polyethylene.
- **Release liner-** Protects the patch during storage. The liner is removed prior to use.
- Other excipients like plasticizers and solvents.

VARIOUS TYPES OF TRANSDERMAL PATCHES:

- **Single-layer Drug-in-Adhesive:** The medication is contained in this system's sticky layer. The adhesive layer in this kind of patch releases the medication in addition to holding the system as a whole and the individual layers to the skin together.

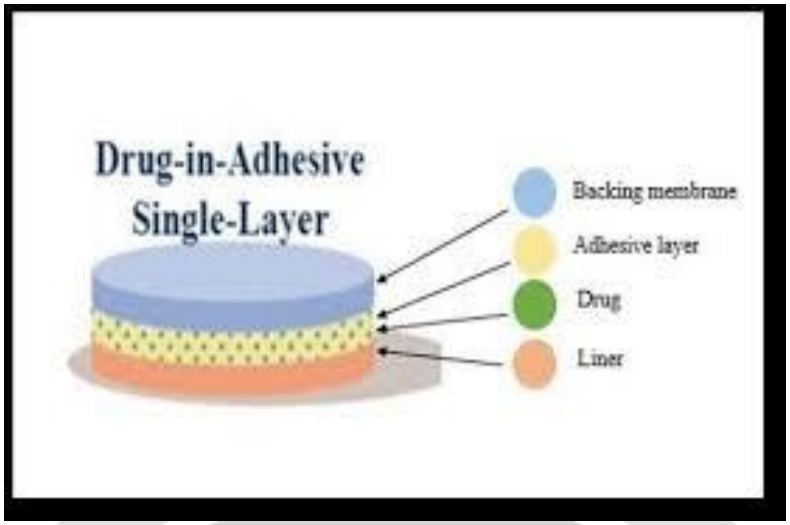


Fig-1 Single layer drug in adhesive

- **Multi-layer Drug-in-Adhesive:** In that both adhesive layers are in charge of the drug's release, the multi-layer drug-in adhesive patch and the single-layer system are comparable. The first layer allows for the drug's instantaneous release, while the second layer regulates the drug's release from the reservoir. The multi-layer method differs, though, in that it incorporates an additional drug-in-adhesive layer, typically divided by a membrane.

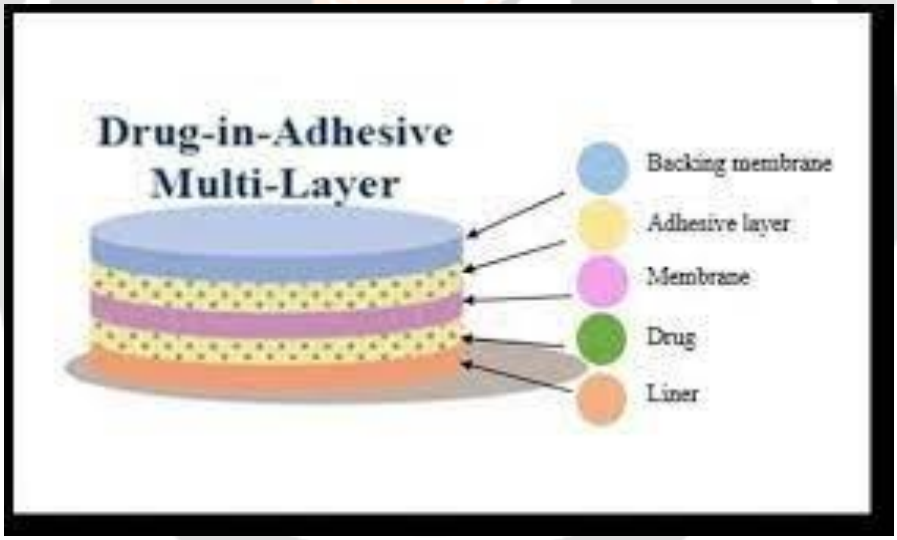


Fig-2 Multi-layer drug in adhesive

- **Reservoir:** A distinct drug layer exists in the reservoir transdermal system, in contrast to the single-layer and multi-layer drug-in-adhesive systems. The drug layer is an adhesive-separated liquid compartment that holds a drug solution or suspension. The backing layer also supports this patch. The rate of release in this kind of system is zero order.

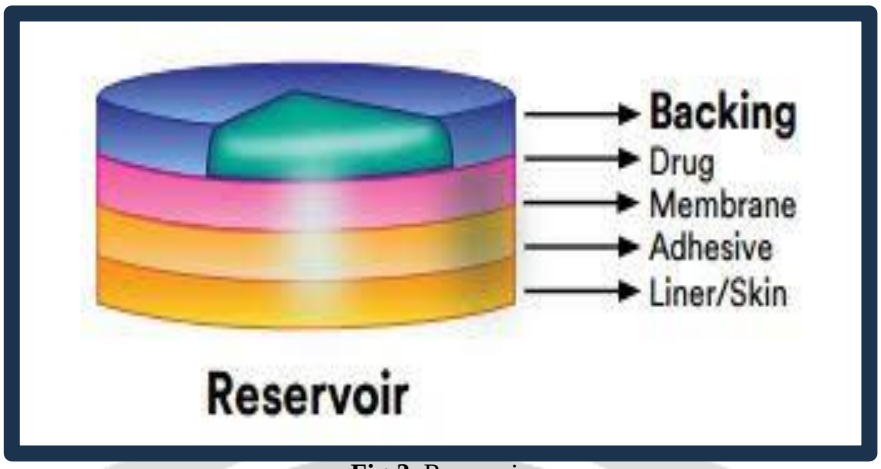


Fig-3 Reservoir

- **Matrix:** A semisolid matrix containing a drug solution or suspension makes up the drug layer of the Matrix system. This patch has a layer of adhesive covering the medication layer to some extent. Also called a monolithic apparatus.

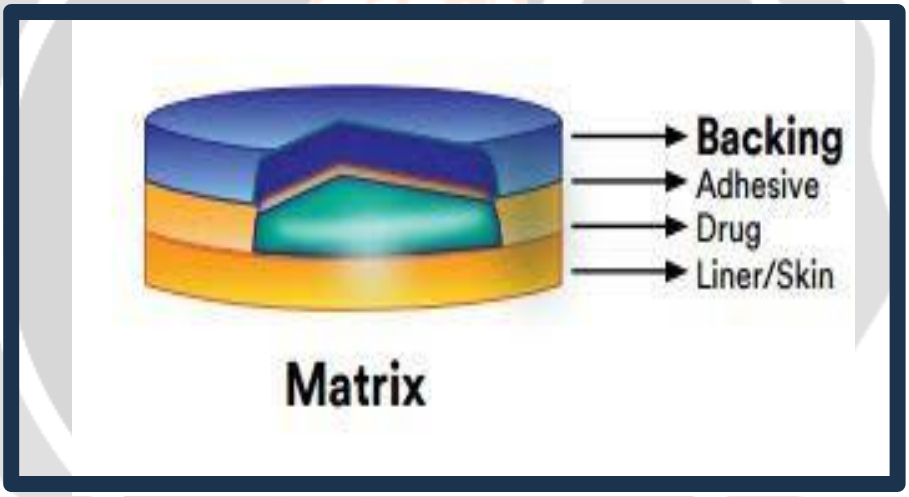


Fig-4 Matrix

- **Micro needle transdermal system:** A micro needle (MN) is a tiny needle that has a height of 10–2000 μm and a width of 10–50 μm. It may easily and painlessly pierce through the epidermal layer and reach dermal tissue. Transdermal drug delivery systems (TDDS) frequently employ micro needles due to its effectiveness, safety, ease of use, and lack of discomfort. There are four varieties of microneedles based on their morphology: hollow microneedles, coated microneedles, dissolving microneedles, and solid microneedles.

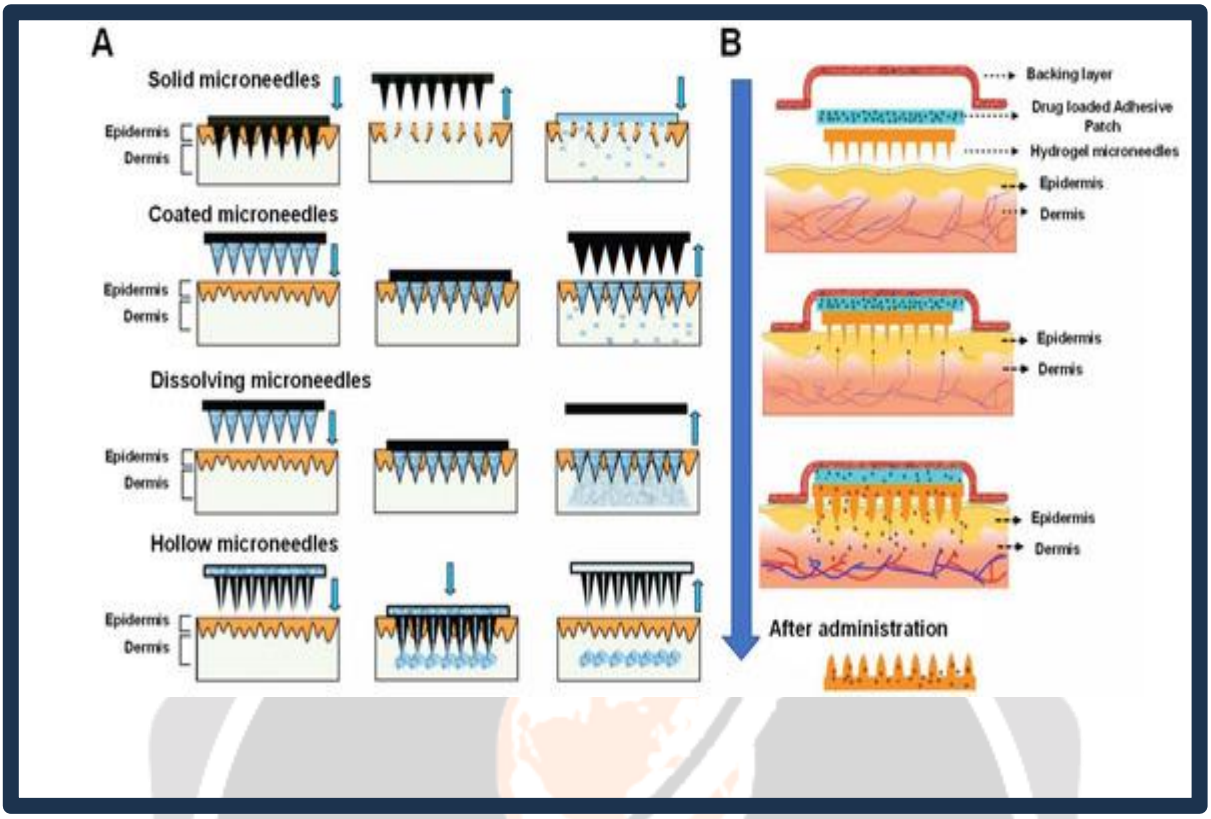


Fig-5 Micro needle transdermal system

Advantages:

1. It is just necessary to utilize this simple process once a week. Such a simple dosing plan can help patients adhere to their pharmaceutical regimen more consistently.

2. Patients who are unable to tolerate oral dosage forms can be accommodated with an alternative mode of administration: transdermal medication delivery.

3. For patients who are unconscious or experiencing nausea, it is quite advantageous.

4. Since transdermal distribution avoids direct effects on the stomach and intestine, medications that disturb the digestive system may be suitable candidates for this mode of administration.

5. Medications that are broken down by the stomach's acids and enzymes could also be worthwhile targets.

6. First pass metabolism, an additional limitation to oral drug delivery, can be avoided with transdermal administration.

Disadvantages:

1. Possibility of local irritation at the site of application.

2. Certain excipients in the patch formulation, the adhesive, or the medication itself may induce erythema, irritation, or local edema.

3. May cause allergic reactions.

4. A molecular weight less than 500 Da is essential.

5. A log P (octanol/water) of 1 to 3 is necessary for permeate to cross the SC and underlying aqueous layers, indicating sufficient aqueous and lipid solubility.

A Brief Review of Skin Structure:

The skin, which makes up 16% of an average person's total body mass, is the largest and most accessible organ in the body, covering 1.7 m^2. The skin's primary purpose is to act as a barrier of defense between the body and the outside world, keeping out germs, toxins, allergies, ultraviolet (UV) radiation, and water loss. The three primary layers of skin are the dermis, which is the middle layer, the stratum corneum-containing epidermis, the outermost layer, and the hypodermis, which is the innermost layer.

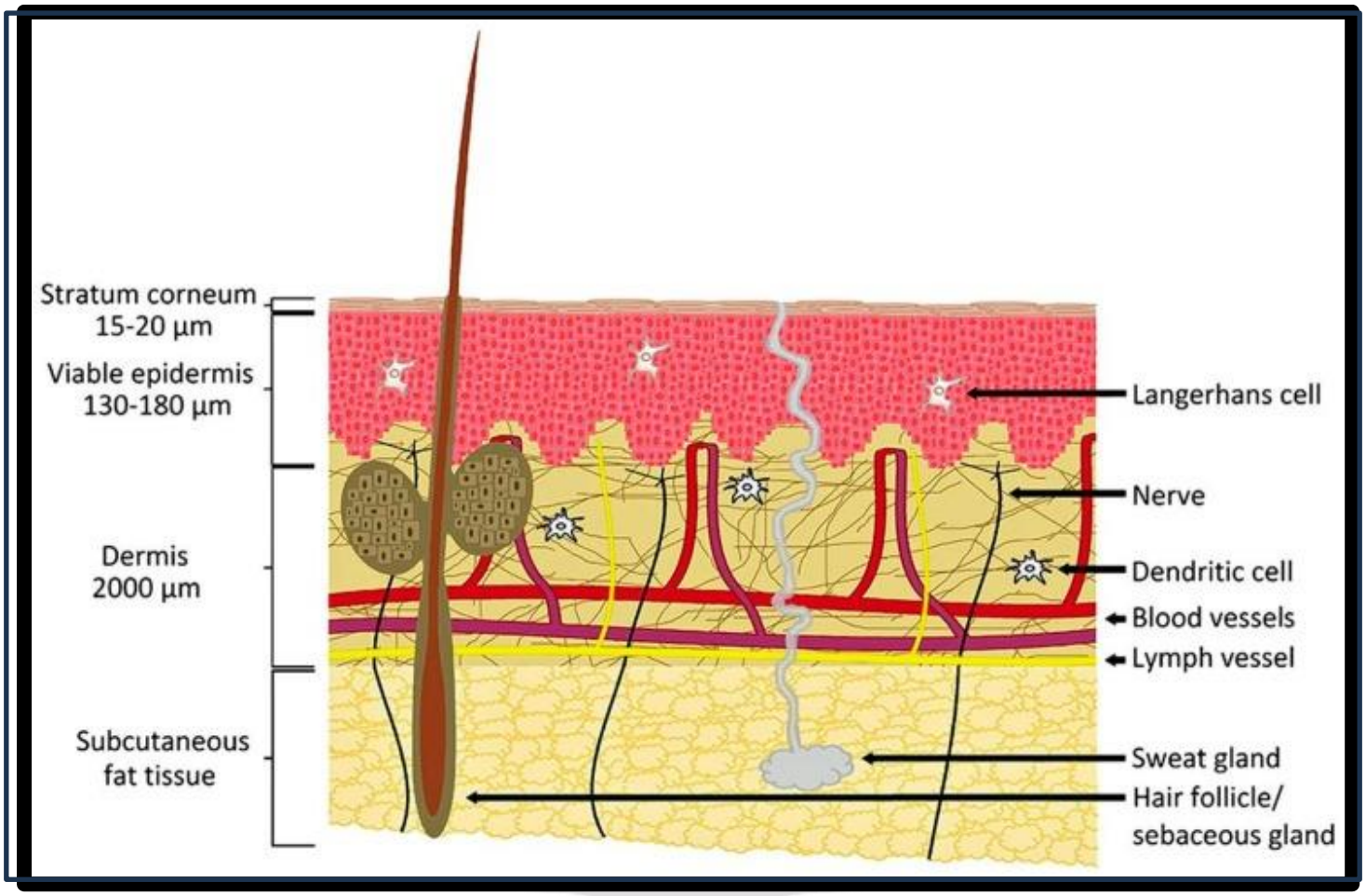


Fig-6 Structure of Skin

Drug Penetration Routes:

There are two probable routes of drug penetration over the intact skin, namely the trans epidermal and trans appendegeal channels. The trans epidermal pathway involves the passage of molecules through the stratum corneum, an architecturally diverse, multi-layered and multi-cellular barrier. It is possible to refer to Tran's epidermal penetration as intra- or intercellular. The intra-cellular pathway through corneocytes, terminally developed keratinocytes, permits the transfer of hydrophilic or polar solutes. Transport via inter-cellular spaces allows diffusion of lipophilic or non-polar solutes through the continuous lipid matrix. Molecules travel through sweat glands and across hair follicles via the trans appendegeal route.

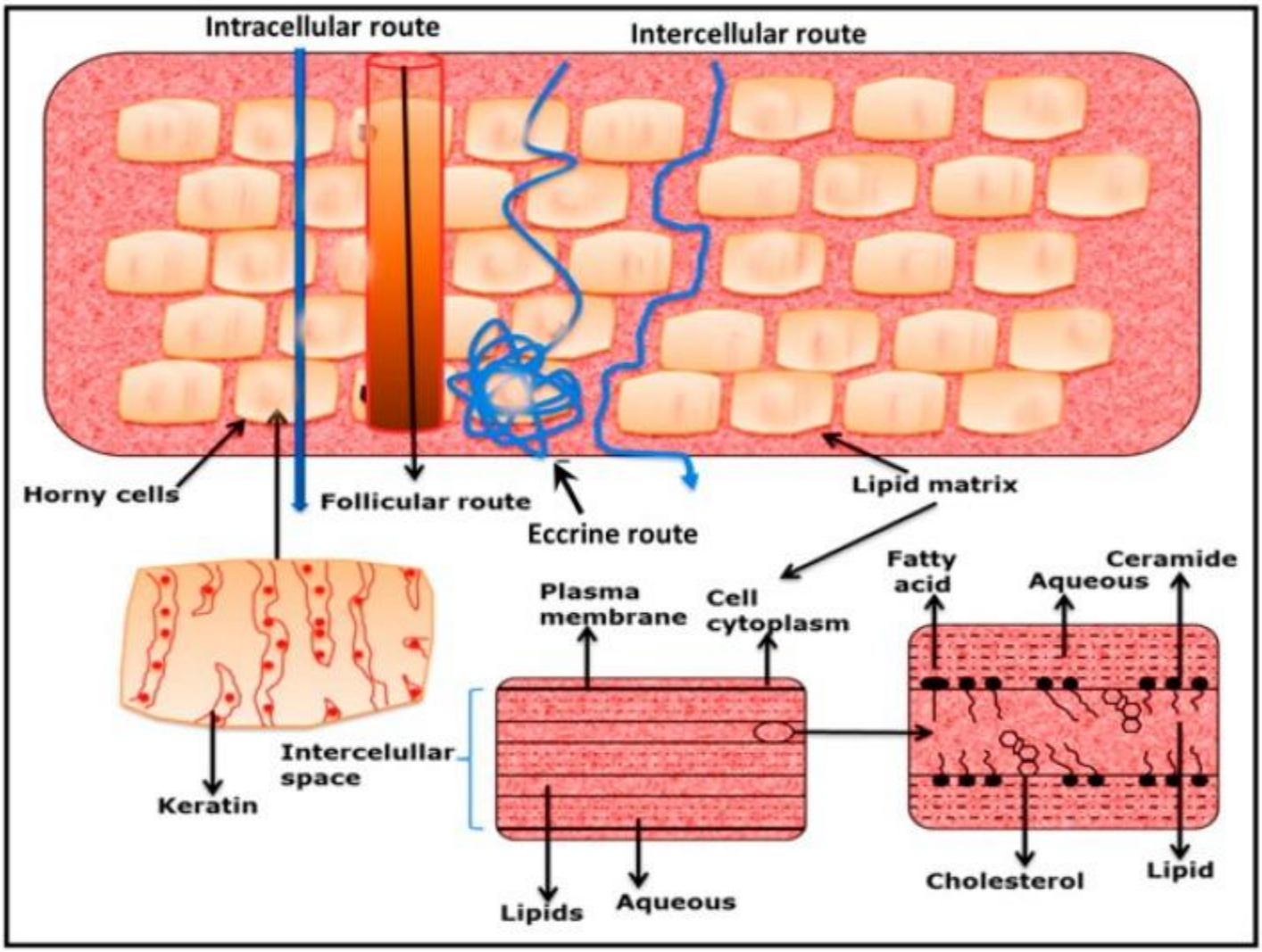


Fig-7 Drug penetration Routes

DICLOFENAC SODIUM:

Diclofenac is an FDA-approved drug used in the treatment and management of acute and chronic pain associated with inflammatory conditions, especially those involving the musculoskeletal system. These include osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Topically, it can treat actinic keratosis. Diclofenac is also FDA approved for ophthalmic administration for the extraction of cataracts, pain in the eye, and photophobia. It is a non-steroidal anti-inflammatory drug (NSAID) and, although it can help to manage the symptoms of pain during inflammatory processes, it cannot reverse or prevent chronic joint damage seen with osteoarthritis and rheumatoid arthritis. Diclofenac was synthesized in 1973 and is the most widely prescribed NSAID worldwide.

MATERIALS AND METHODS:

ACTIVE INGREDIENT: The chemical, biological material, or any other entity or component that is in charge of the therapeutic (pharmacological, physiological, physical, etc.) effects in a product, like a vaccination, is known as an active pharmaceutical ingredient, or API.

DICLOFENAC SODIUM: A well-known nonsteroidal anti-inflammatory drug, diclofenac is frequently used to treat musculoskeletal conditions, arthritis, toothaches, dysmenorrhea, and other conditions by providing symptomatic pain and inflammation alleviation.

PLASTICIZER: Transdermal plasticizers enhance the patch's look, facilitate film formation, and lessen the likelihood of cracking. Additionally, they can lengthen the patch's folding endurance, boost its tensile strength, and make it more flexible. Plasticizers may also have an impact on the patch's ability to stick. As an illustration, consider propylene glycol (PG), polyvinyl alcohol (PVA), and polyvinyl pyrolidone (PVP).

PENETRATION ENHANCER: Chemical substances known as penetration enhancers can help active pharmaceutical ingredients (API) pass through or into biological barriers with low permeability. These substances are added to pharmaceutical formulations in order to improve the absorption of active pharmaceutical ingredients (APIs) during transdermal and transmucosal drug administration (such as in the eyes, nose, mouth, and buccal regions). Usually, they pierce biological membranes and cause a reversible loss in their barrier qualities.

BACKING AGENT: They are flexible and provide a good bond to the drug reservoir, preventing the drug from leaving the dosage form from the top. It is an impermeable membrane that protects the product during its use on skin.

SOLVENT: In transdermal drug delivery systems, a solvent plays a crucial role in facilitating the delivery of drugs through the skin. Here are some key functions of a solvent in transdermal drug delivery:

1. Dissolving the drug: The active pharmaceutical ingredient (API) is dissolved by the solvent, enabling uniform dispersion of the API throughout the formulation.

2. Improving drug stability: Solvents can help stabilize the drug, preventing degradation or oxidation.

3. Controlling drug release: In order to guarantee a consistent and regulated distribution, solvents can affect the transdermal system's drug release rate.

5. **Facilitating formulation:** Solvents facilitate the production of a consistent formulation, which facilitates the transdermal system's application and manufacturing.

Materials:

- **ACTIVE INGREDIENT:** Diclofenac Sodium
- **PLASTICIZER:** Polyvinyl alcohol (PVA), Polyvinyl pyrolidone (PVP), 7Propylene glycol (PG)
- **PENETRATION ENHANCER:** Dibutyl phthalate (DBP) Propylene glycol (PG)
- **BACKING AGENT:** Ethyl cellulose (EC)
- **SOLVENT:** Chloroform and Methanol

METHOD OF PREPRATION:

The polymer was dissolved in chloroform: methanol (1:1) solvent.

↓

The drug (Diclofenac Sodium) was dispersed uniformly in the viscous solution with continous stirring.

↓

The resulting mass was poured into levelled mercury surface in a petri dish covered with inverted funnel.

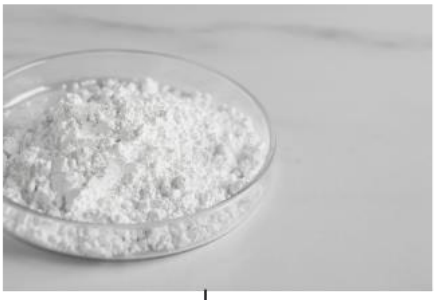
↓

The petri dish was left undisturbed at room temperature for one day.

↓

The patch was obtained intact by slowly lifting from the petri dish and transdermal patches were cut into radius of 2cm.

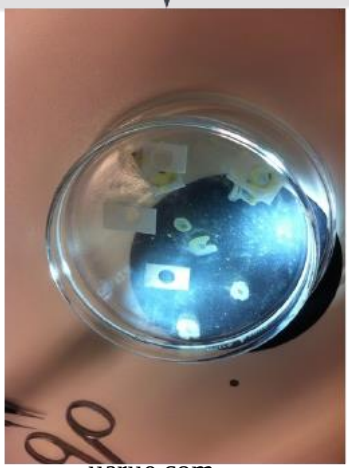
Chloroform and Methanol



Diclofenac and Polymers

Thick mass poured in petri dish

Patches cut into radius of 2cm



Diclofenac sodium patches

EVALUATION PARAMETERS

- **Patch thickness:** The thickness of the drug-loaded patch is measured at multiple locations using a digital micrometer, and the average thickness and standard deviation are used to guarantee the thickness of the final patch. Transdermal film thickness can be measured at various locations on the film using a micrometer, screw gauge, or traveling microscope dial gauge.
- **Weight uniformity:** The generated patches are dried at 60°C for four hours prior to testing. It is necessary to divide a set patch area into multiple portions before weighing each section with a digital balance. The individual weights must be used to get the average weight and standard deviation values.
- **Folding endurance:** An area-specific strip is to be cut uniformly, then folded in the same spot repeatedly until it breaks. The number of times a film can be folded in the same direction without breaking is used to calculate its folding endurance.
- **Percentage Moisture content:** The produced films must be weighed separately and stored for 24 hours at room temperature in desiccators filled with fused calcium chloride. The following formula must be used to reweigh the films after 24 hours in order to determine the percentage moisture content:

  % Moisture content = Initial weight – Final weight X 100 \Final weight
- **Content uniformity test:** Ten patches are chosen, and each patch's content is decided. Transdermal patches pass the content uniformity test if nine out of ten have material that falls between 85% and 115% of the given value, and one patch has content that falls between 75% and 125% of the specified value. However, an additional twenty patches are tested for drug content if three of the patches have content within the range of 75% to 125%. The transdermal patches pass the test if the range of these 20 patches is between 85% and 115%.
- **Moisture Uptake:** For a full day, weighed films are stored at room temperature in desiccators. Once a constant weight is achieved, they are taken out and put in desiccators with saturated potassium chloride solutions at 84% relative humidity. Here's how the percentage of moisture uptake is calculated

  % moisture uptake = Final weight – Initial weight X 100\ Initial weight
- **Drug content:** In a set volume of a suitable solvent, a predetermined patch area must dissolve. Subsequently, the combination needs to be filtered via a filter medium before the relevant technology (UV or HPLC) is used to evaluate the drug's composition. Any given value represents the average of three different samples.

Conclusion

The development and analysis of transdermal Diclofenac Sodium patches demonstrate the potential of transdermal drug delivery systems as an effective alternative to traditional oral and topical formulations. Through careful selection of polymers, such as hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA), and plasticizers like glycerin, the patches provided a controlled and sustained release of Diclofenac Sodium over an extended period. The inclusion of permeation enhancers, like propylene glycol, improved the drug's ability to penetrate the skin, enhancing its therapeutic efficacy.

Physicochemical evaluations revealed that the patches exhibited good mechanical properties, including tensile strength, flexibility, and uniformity in thickness and weight, which are essential for patient comfort and consistent drug administration. Drug release studies showed a correlation between polymer composition and release kinetics, with certain formulations offering a more prolonged release profile, reducing the need for frequent dosing.

Overall, the study concluded that the composition of the transdermal patches plays a critical role in drug release behavior and skin permeation. Optimizing the polymer matrix and excipients is key to enhancing the performance of transdermal systems. These findings highlight the potential for transdermal Diclofenac Sodium patches to improve patient outcomes by providing a convenient, non-invasive, and efficient method of pain management.

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