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Research Paper

Formulation and Evaluation of Transdermal Patch of Ibuprofen

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Abstract:
When transdermal medication are used, the medication is usually administered subcutaneously via a transdermal delivery system. To overcome this drawback, ibuprofen transdermal patches have been developed and evaluated. In this study, polyvinylpyrrolidone (PVP) and ethylcellulose polymer matrices were used to produce ibuprofen transdermal patches. To evaluate the effectiveness, weight consistency, thickness, drug content, and in vitro drug diffusion of ibuprofen transdermal patches.
These reviews showed that all designs worked well. After 180 minutes of in vitro diffusion using a Franz diffusion cell in phosphate buffer PH7.4,1.7083mg/cm^2 of ibuprofen was emitted.

Keyword: *Ibuprofen, PVP, transdermal patch.*

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I. Introduction

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) used for pain, relief, and fever. Oral administration as gastrointestinal symptoms.

These side effects may increase with the use of additional medications. In the recommended form, such products need to be injected at least three times a day, while in the extended-release from, the dosage should be taken twice a day due to greater metabolism and shorter elimination half-life in the former drugs. Negative side effects such as abdominal pain, nausea, vomiting, headache and adaptation problems may occur due to long-term use of the drug in the treatment of rheumatoid arthritis. The lower daily dose makes it a candidate for the development of an effective transdermal system that will eliminate first-pass metabolism, increase plasma-concentrations, reduce side effect such as stomach pain, and assist with follow-up. Benefits of transdermal delivery include increased bioavailability by bypassing primary hepatic metabolism.[1]

Transdermal delivery systems are self-contained local drug applications in the form of patches that delivery, drugs at a predetermined and controlled rate according to their effects in the body Transdermal drug delivery, drugs can easily pass through the skin and enter the joints to show their effects.[2]

A transdermal patch is defined as an adhesive cream placed on the skin to fully deliver the drug through the skin to the blood vessels of the pre-release system to obtain it in the body.[3]

Most transdermal system on the market today usually take the form of a semi-permeable membrane called a patch.Transdermal Drug Delivery System(TDDS), also known as

"Transdermal patches" or "skin patch" are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin and blood.[4]
Transdermal drug delivery system (TDDS)allowthe delivery of available drugs into the systemic circulation at a controlled rate through the skin layer.[5]
Ibuprofen belongs to the class of propionic acid derivatives, has analgesic, anti-inflammatory and antipyretic effects, is used only in the treatment of inflammatory diseases, osteoarthritis, rheumatoid arthritis, mild to severe pain. Taking ibuprofen by mouth may cause some gastrointestinal bleeding, abdominal pain, diarrhoea, nausea, vomiting.[6] Ibuprofen is a prostaglandin synthase inhibitor. Its molecular formula is C13H18O2 and its molecular weight is 206.28.

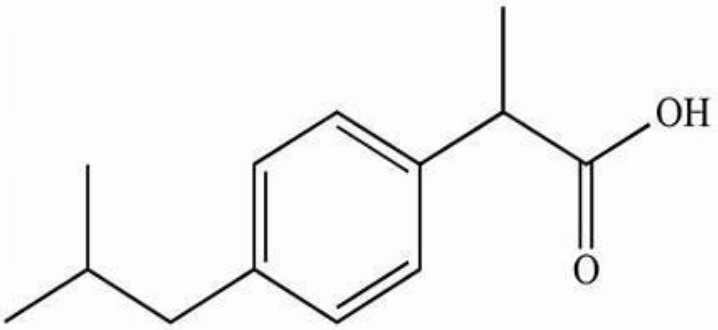


Figure 1: Structure of Ibuprofen

Advantages:
1.Hepatic first pass metabolism, salivary metabolism and intestinal metabolism are excluded.
2.Medicine that cause irritation and enable the absorption of intestinal bacteria can be conveniently used through the skin.
3.Patient compliance increases due to decreased frequency.
4.Treatment failure associated with regular doses of conventional treatments can be prevented.
5.Adverse effects are minimized due to the stable and visible blood pressure-time profile.
6.The risks, pain and discomfort associated with parenteral therapy are avoided.
7.The release time is longer than oral continuous.

Disadvantages:
1.One or more ingredients in the formula may irritate the skin.
2.Binding of the drug to the skin may lead to drug waste.
3.It should only be used in chronic conditions that require long-term medication, such as high blood pressure, angina and diabetes.
4.Market time is variable and can range from hours to days for different drug candidates.
5.It cannot distribute drugs throughout the body.
6.Transdermal treatment is not possible for ionic drugs.
7.Transdermal therapy only works with some strong medications.

Structure of skin:

Skin can be thought of as having four different tissue layers, including non-living epidermis, living epidermis, living dermis, and subcutaneous tissue. Epidermis is the thin, tough outer layer of the skin. The epidermis contains keratinocytes. They arise form cells in the deepest layer of the epidermis, called the basal layer. New keratinocytes gradually migrate upwards towards the epidermal surface. The stratum corneum is the outer layer of the epidermis and is waterproof; if not damaged, it prevents most bacteria, viruses and other

foreign substances from entering the body. The thickness of the active epidermal layer of the skin is approximately 50-100 um. The humidity rate is approximately 90%. The next layer of the skin, the dermis, is a thick layer of fibrous and elastic tissue that gives the skin flexibility and strength. The dermis contains blood vessels, sweat glands, sebaceous glands, hair follicles and blood vessels.[7]

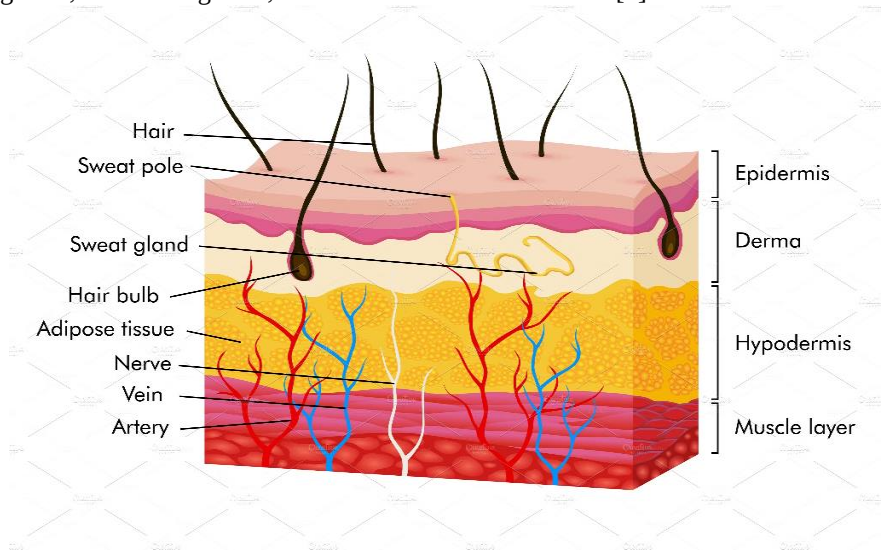


Figure 2:Structure of skin

Pathways of skin permeation:

Chemical molecules enter the skin through a variety of pathways, including sweat ducts, hair follicles, and sebaceous glands, or directly through the stratum corneum.[8] For the last few years, scientists have debated about the importance of transport of the shunt or extension across the cuticle, and this is exacerbated by the lack of suitable experimental models. Stratum corneum consists of 10 to 15 layers of keratinocytes.[9]

Types of transdermal patches:

Transdermal patches generally fall into four categories: drug-in adhesive, reservoirs, matrix, and micro-reservoir system are illustrated in figure 3.

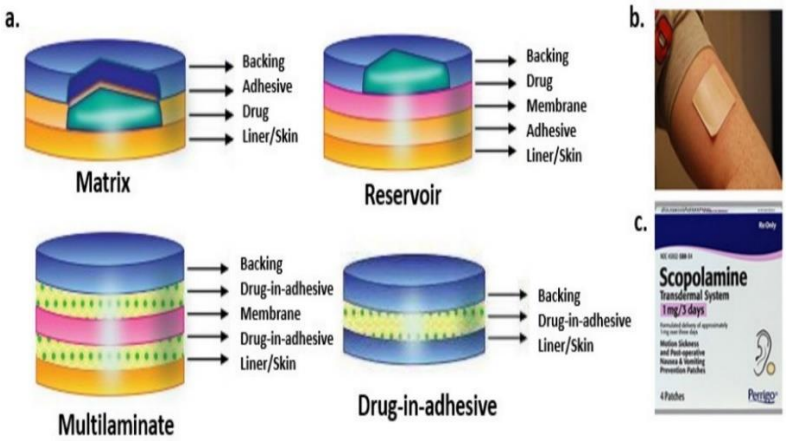


Figure 3: Transdermal patches

Single layer drug in adhesive

This type of adhesive contains chemicals. The adhesive not only holds the layers together, but is also responsible for releasing the medicine on to the skin. The adhesive layer is surrounded by temporary padding and backing.

a. Multi-layer drug in adhesive:

This type is similar to a layer, but has an immediate release drug, and other systems can provide controlled release with an adhesive layer. The adhesive layer is responsible for the release of the drug. The patch also has temporary patches and permanent support.

b. Reservoir system:

In this case, the drug reservoir is embedded between an impermeable backsheet and the rate control membrane. The drug is released only through the price control membrane, which may be microporous or nanoporous. In the drug reservoir compartment, the drug may be in the form of a solution, suspension, gel, or dispersed in a solid polymer matrix.

c. Matrix system:

- **Drug-in-adhesive system:**

This type of patch is made by mixing a chemical with an adhesive to create a chemical reservoir. It is then spread through the impermeable process again by heavy casting or melting. The upper part of the reservoir is protected by a layer of adhesive polymer without intermediates. It can be divided into single-layer and multi-layer cream. The system is considered to be compatible with many drugs. It has advantage of reducing size and thickness.

- **Matrix-dispersion system:**

The drug is separated in a hydrophilic or lipophilic polymer matrix. It is then transformed into a medicine container of certain shape and thickness. The polymer containing the drug is attached to the occlusive substrate within a chamber made of a drug-impermeable backsheet.

- **Micro-reservoir system:**

The system consists of microscopic spheres that are drug reservoirs and release the drug at a zero dose to maintain a constant drug level. Micro-reservoir systems are a combination of reservoir and matrix dispersion systems. A water-soluble polymer solution is mixed with the drug to create a reservoir.[10]

II. Material And Methods:

Material:

Ibuprofen was received as a gift sample from sky Lab Pvt Ltd, Rohak, Ethyl cellulose, polyvinylpyrrolidone, polyethylene glycol 400 were received as a gift sample.

Methods:

Determining the maximum wavelength of ibuprofen:

The maximum wavelength of ibuprofen was determined by measuring the absorbance of 10 u g/mL of ibuprofen solution in PH 7.4 phosphate buffer solution. By measurement, it was determined that the maximum wavelength of ibuprofen was 222nm.

Determination of calibration curve of ibuprofen:

The ibuprofen treatment is then diluted in PH 7.2 phosphate buffer to yield a series of dilutions containing 4,6,8,10,12, and 14 ug of ibuprofen per milliliter of solution.The absorbance of the above dilutions was measured on a UV-visible spectrophotometer at 221nm and 255.8 nm.

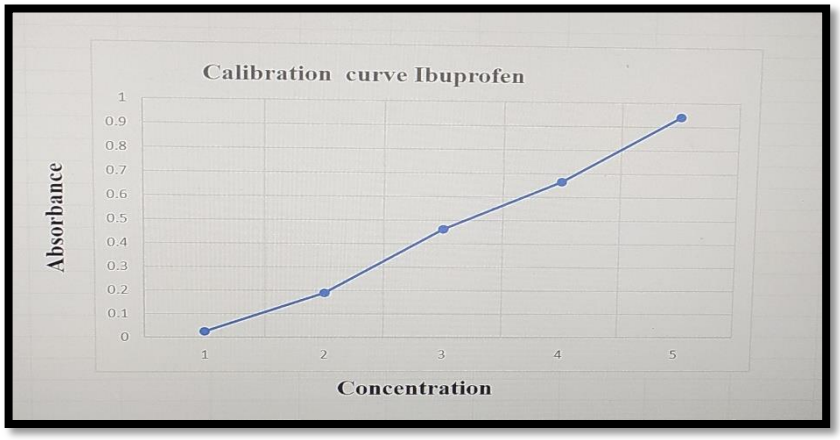


Figure 4: Calibration curve of ibuprofen

Preparation of Transdermal Patches:

1]Dissolve the weight of ethylcellulose (630,720,540,810mg), PVP (270,180,360,90mg) in ethanol (4ml) and let it swell for 15 minutes.

2]Ibuprofen was dissolved in toluene (16ml) and added to the polymer solution.

3]Add PEG to the top and continuously stir on magnetic stirrer.

4]Add the contents and sonicate the air trap for approximately 10 minutes

5]pour the above solution into a petri dish with aluminium foil and evaporate the solvent at room temperature for 8 to 12 hours.
6]Ibuprofen has analgesic and antipyretic activity. As with other NSAIDs, its mode of action is not fully understood but may involve prostaglandin synthase inhibition.

Figure 5: Formulation of patch

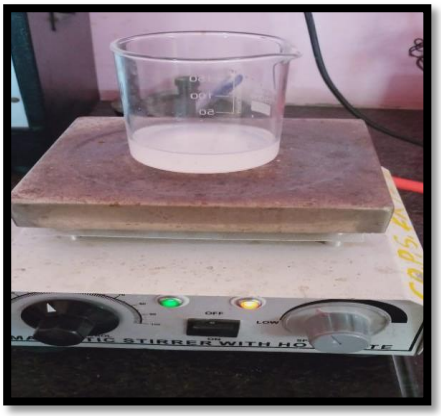


Figure 6: Using magnetic stirrer for make stir bar.

Table 1: Preparation of the trial patches with different concentrations of different polymers.
Evaluation of Transdermal Patch

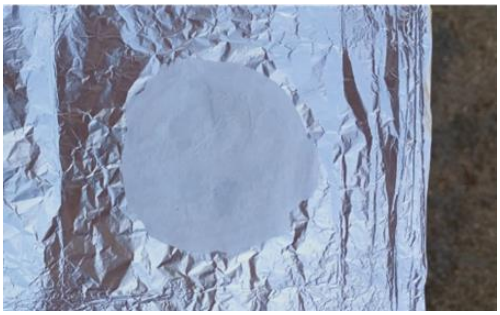
Patch No.	**Patch A**	**Patch B**	**Patch C**
Ingredients	mg/patch	mg/patch	mg/patch
Ibuprofen	100	100	100
Ethyl cellulose:PVP	630:270	720:180	810:90
Toluene:ethanol	16ml:4ml	16ml:4ml	16ml:4ml
Polyethylene glycol	0.3ml	0.3ml	0.3ml

Drug content analysis:

Cut the transdermal membrane of one area (7,065 cm^2) into small pieces, dissolve in 50 ml of phosphate buffer pH 7.4 and sonicate for 5 min. The chemical sample was filtered through Whatman filter paper and the filter was placed in a 100 ml volumetric flask. Then, the volume was completed to 100 ml with phosphate buffer pH 7.4 remove 1 ml of the above solution and dilute to 100 ml with phosphate buffer (pH 7.4). Absorbance is measured at 222.6 nm and 255.7 nm.

Thickness:

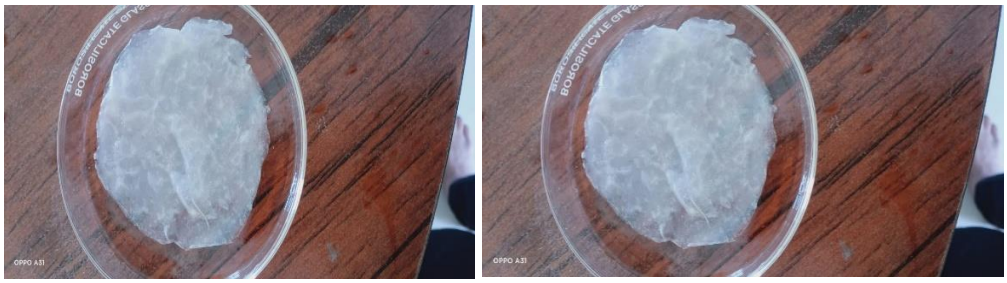
Patch thickness of three different patches was measured using a digital caliper and the average of the three readings was calculated. [11] Cut the patch of the surface area into slices and weight accurately, transfer the explosives to a beaker filled with phosphate buffer pH7.4 and sonicate the beaker for 8-12 hours, filter the contents of the beaker and check the drug in solution compared to placebo in the 257nm test.[12]



Thickness of Patch

Moisture loss:
The weighted film of each design was stored in a desiccator and exposed to 98% humidity media at room temperature and weighed after 3 days. Record the average of three readings and calculate the percentage of moisture used.[13]
% Moisture Uptake = (Final Weight – Initial Weight / Initial Weight) x100

Weight Variation:
For weight loss, three pieces ($4cm^2$) from three difference areas were selected, cut and measures on electronic balance. The testing is done to check consistency of weight and hence the difference between products.[14]



Patch No.1Patch No. 2

Diffusion Study:
A solution optimal for in vitro drug diffusion and physical stability when stored for 28 days was used. This diffusion experiment uses a modified pump, a magnetic stirrer, a glass beaker, a water batch, a receiver chamber, a thermometer, and a hose witha thermometer. Use the membrane as a filter and phosphate buffer at pH 7.4 as the diffusion medium. A transdermal area(7,065 cm^2) was placed over the membrane and in contact with the receptorcompartment containing pH7.4 phosphate buffer. Use a magnet to continuously stir the diffusion medium and maintain the temperature at $37\pm0.5\ ^oC$. The sample is removed from the receiver chamber at regular intervals (5,10,15,20,30,60,90,120 minutes) and replaced with an equal amount of fresh sterile solution (3 minutes). The duration if the test is 3 hours. Samples were analyzed for chemical content using spectrophotometry at 222.6 nm and 255.7 nm. Drug release was calculated with the help of a standard calibration curve, and then the percentage of drug release was calculated.[15]

III. Discussion:

Three batches of transdermal patches were prepared using maximum and minimum concentrationsof ethyl cellulose and polyvinylpyrrolidine (PVP). Various effects of ethylcellulose and PVP on drug release have been documented. The results showed that the patch achieved maximum release or exposure when the maximum ethylcellulose: PVP ratio used in patch B was 8:2. Among the three different groups, Patch B showed the highest release because the ethylcellulose ratio in patch B was 8:2. In area A,the ethylcellulose:PVP ratio is 7:3, in area C, the ethylcellulose: PVP ratio is 6:4. Remove the patch and sand it between the filters and place it between the two parts of the diffusion cell. Place pH 7.4 phosphate buffer into the receptor chamber. Place the entire assembly in the magnetic machine and perform the test at 37 ^oC for 24 hours. At each interval, 5ml of sample was collected and replaced with an equal amount of buffer. Measure the concentration in the sample using a UV double beam spectrophotometer at 222nm. Calculate the rate of diffusion of the drug based on the ibuprofen formula. Calculate the amount of the drug and draw a graph with the x-axis as time and the y-axis as cumulative amount.

IV. Conclusion:

Threeibuprofen patches were prepared and the effects of different polymers such as ethylcellulose and PVP wereanalyzed. If the concentration of ethylcellulose increases, the output also increases. After all physicochemical tests, diffusion kinetics were determined for all patches and then all kinetic models(A,B,C)were studied for the patch.

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