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EVALUATION OF FORMULATED TRANSDERMAL PATCHES

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Abstract
The goal of this study was to use the solvent casting process to create a matrix-type transdermal treatment system comprising the medication aceclofenac and various ratios of hydrophilic (hydroxyl propyl methyl cellulose) and hydrophobic (methyl cellulose) polymeric systems. The physical characteristics of developed transdermal patches were assessed, including their thickness, weight fluctuation, medication content, flatness, tensile strength, folding durability, moisture content %, and water vapour transfer rate. In this work, Cefdinir was utilized to make transdermal patches out of a variety of polymers, including Cellulose derivatives, polyvinyl alcohol, polyethylene, polypropylene, polyvinylpyrrolidone, and polymethyl methacrylate, all of which had varying concentrations. Using PEG-400 as a plasticizer, patches were created using the solvent evaporation process. Transdermal films that had been developed were tested physically for things like thickness, weight fluctuation, drug content, flatness, tensile strength, folding endurance, and moisture content as a percentage. The physical stability of all developed formulations was satisfactory.

Keywords: Transdermal Patch, In vitro drug study, Transdermal

INTRODUCTION

There has been a transdermal medicine delivery technology for a very long time. The most widely used methods for dermatological problems in the past were topically administered lotions and ointments. Systemic adverse effects are common with some of these formulations, which is an indication of skin absorption. Several medications have been rubbed on the skin as systemic treatments. The phrase "transdermal delivery system" broadly refers to any medicine formulation applied topically with the goal of releasing the active component into the bloodstream. Transdermal therapy systems have been created to provide regulated continuous medication administration to the systemic circulation via the skin. Additionally, it avoids a number of negative side effects include painful medication administration and the drug's first-pass metabolism that occurs when using conventional drug delivery methods. Therefore, there has been a lot of interest in this transdermal medication delivery technology recently. Liners, adherents, drug reservoirs, and drug release membrane are some of the parts of a transdermal patch that are essential for the medication's release through the skin. To distribute the medicine from the transdermal patch, many kinds of patches and application techniques have been developed.

Compared to other methods of medication administration, transdermal drug delivery offers a few benefits that promote patient compliance. This device is most suited for systemic drug administration during 24-hour periods because to its non-invasive nature, simplicity of application and removal, predefined rate of drug penetration, enhanced bioavailability of medication, and lower hepatic metabolism.

LITERATURE REVIEW

Akanksha d. Taware et.al (2023) A method for medication absorption via the skin is the transdermal drug delivery system. The system offers a number of benefits over traditional delivery methods for systemic and local medication delivery with straightforward administration, such as intravenous or oral administration. The fundamental goal of transdermal drug delivery systems is to deliver medications into the bloodstream via the skin at a predefined pace with the least amount of interpatient variation possible. Cefixime is often a powerful antibiotic since it is actively employed against a wide range of bacteria. In many different areas of the body, cefixime is used to treat bacterial infections. It is a member of the cephalosporin antibiotics drug class. It functions by eradicating germs or stopping their development. However, this medication won't help with the flu, the common cold, or any other viral diseases. Cefixime 200 mg tablet transdermal patches are created utilizing 50 mg of the medication to prevent negative effects from the oral route.

K. Sravanthi et.al (2020) The goal of this study was to create a matrix-type transdermal treatment system for the medication aceclofenac using a solvent casting approach with various ratios of hydrophilic (hydroxyl propyl methyl cellulose) and hydrophobic (methyl cellulose) polymeric systems. The physical properties of developed transdermal patches, including thickness, weight variation, medication content, flatness, tensile strength, folding durability, moisture percentage, and water vapour transfer rate, were assessed. Good physical stability was shown by all produced formulations. The formulations of drugs were studied in-vitro using Franz diffusion cells. The results followed the mixed zero-order release profile of aceclofenac. However, the release profile of the improved formulation F9 (99.500.09) showed that a diffusion mechanism controlled the drug's penetration through the patches. Formulation F9 had the greatest flux of any formulation and 217 7, 42-fold increases in drug permeation.

Adhikrao Vyankatrao Yadav et.al (2018) The goal of the current study was to create a transdermal delivery system for lornoxicam utilizing Tween 20 as a permeation enhancer and chitosan as a rate-controlling polymer. Then, assess how Tween 20 affects the physicochemical characteristics of the patches and how well drugs permeate the membrane. Methods: Solvent casting was used to create transdermal Lornoxicam patches. Physical and chemical properties of the produced patches were assessed, including tests on in vitro drug release and skin sensitivity. FTIR, DSC, and XRPD techniques were used to study the interaction between the medication and polymer. Results: Formulation L4 with a greater concentration of Tween 20 demonstrated 74.6% diffusion in 12 hours and adhered to Korsmeyer-Peppas drug release kinetics. In a skin irritation test, the appropriate formulation failed to exhibit any signs of erythema or edema. Drug and polymer have high compatibility, according to an FTIR research. Conclusion: The developed sustained release matrix transdermal patch formulation of lornoxicam employing chitosan has showed excellent promising outcomes.

Priyanka Kriplani et.al (2017) Transdermal medication administration has significantly improved medical procedures. It is a medical patch that releases a specified dosage of medicine into the bloodstream via the skin. A transdermal patch offers a controlled release of the medication into the patient, typically through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. This is a benefit of transdermal drug delivery over other methods of medication delivery. In the current study, transdermal films containing the non-steroidal anti-inflammatory drug diclofenac sodium were created using the

mercury substrate method and evaluated for physicochemical factors including thickness, weight variation, moisture uptake, moisture content, folding endurance, and drug content values. Three transdermal patches were created utilizing three different ethyl cellulose concentrations. It was determined that patch thickness, weight homogeneity, and folding endurance all increase as polymer concentration does. With a rise in polymer concentration, percentage moisture content and percentage moisture absorption decline.

Kunal N Patel et.al (2012) The goal of this study was to create a matrix-type transdermal medicinal system using acrylic glue and the solvent evaporation method that included the medication Diclofenac acid. The transdermal penetration of diclofenac acid was increased by using various quantities of Labrasol, oleic acid, and triacetin. When making transdermal patches, silicone-coated polyester film is recommended as the release liner and polyethylene monolayer film as the backing membrane. Formulated transdermal patches were physically assessed for drug content, tensile strength, % elongation, folding endurance, thickness, weight change, and percentage moisture absorption. Good physical stability was shown by all produced formulations. Franz diffusion cells were used to conduct investigations on the formulations' in vitro skin permeability. Comparing all formulations, the one with the best in vitro skin permeation through human cadaver skin had 5% medication, 85% adhesive solution, and 10% triacetin as a permeation enhancer. It was discovered that the results rate followed zero order kinetics. These findings suggest that the formulation F3 has shown optimal release in a manner independent of concentration. Studies on medication stability and primary irritation show that the transdermal patches don't cause any irritation after six months.

ADVANCE DEVELOPMENT IN TDDS

The recommended method for passive transdermal drug administration is drug in adhesive technology. Adhesives and excipients are the subject of two fields of formulation study. Adhesive research focuses on personalizing the adhesive to enhance skin adherence during the course of wear, enhance medicine stability and solubility, decrease lag time, and boost delivery rate. The efficacy of the transdermal patch may be improved by tailoring the adhesive chemistry since there is no universal adhesive that can handle all medication and formulation chemistries. The development of transdermal technologies that employ mechanical energy to improve drug flow over the skin by either changing the skin barrier (mainly the stratum corneum) or raising the energy of the drug molecules has been the subject of much study over the last 10 to 15 years. These so-called "active" transdermal technologies include ionophoresis (which uses low voltage electrical current to drive charged drugs through the skin), electroporation (which creates transient aqueous pores in the skin using brief high voltage electrical pulses), sonophoresis (which uses low frequency ultrasonic energy to disrupt the stratum corneum), and thermal energy (which uses heat to make the skin more permeable and to increase the energy of drug molecules). Drug flow through the skin may be increased even with the use of magnetic energy, known as magnetophoresis.

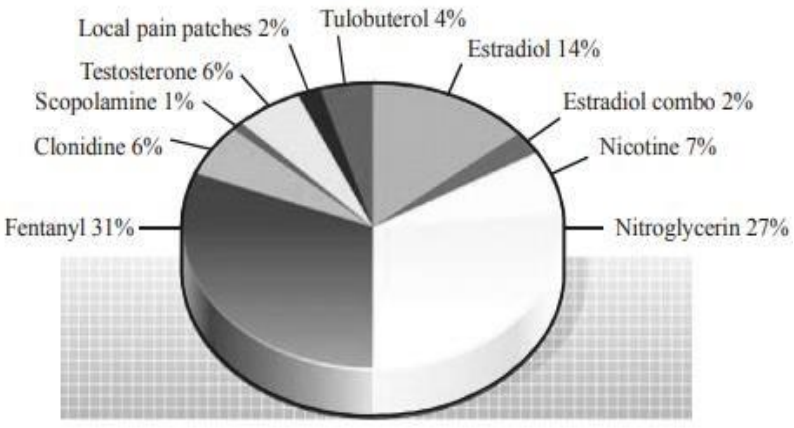

Fig 1: Global TDD product sales by segment

MATERIALS AND METHODS

The following materials were employed in this study: Cefdinir as a medication, PEG-400 as a plasticizer, Polyvinyl Alcohol, Polyethylene, Polypropylene, Polyvinylpyrroli done, and Polymethylmethacrylate as polymers. It was shown that dimethylsulphoxide improved Cefdinir's transdermal permeability. Solvent casting was used during the whole preparation process. Analytical-grade materials were used for all other lab equipment.

Preparation of Transdermal Patches

- Utilizing Cefdinir, plasticizers, and penetration enhancers, the patches were created utilizing the solvent evaporation process. • In a beaker, 5 mg of Cefdinir was dissolved in 5 ml of ethanol. Next, 6 ml of PEG 400 was added.
- The mixture was continually agitated until a solution formed.
- Add 0.5 gm of polymer to the produced solution now, and mix for 10 minutes.
- Finally, increase the amount of the aforesaid solution to 20 ml by adding 2 ml of the penetration enhancer.
- This mixture was well mixed before being put onto a petri dish coated with castor oil.
- To reduce solvent evaporation, a funnel of the appropriate size was inverted over the petri dish. • The casting solvent was then given 48 hours to evaporate to produce dry films.
- Patches were scraped with a knife and cut into uniform pieces of 2 2 cm after 48 hours.
- The patches were kept in a desiccator between wax paper sheets until further examination.

Table 1: Formulations of Transdermal Patches

No.	Ingredients	F1	F2	F3	F4	F5	F6	F7
1	Cefdinir	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
2	HPMC K4M	0.5 gm	-	-	-	-	-	-
3	HPMC K100 M	-	0.5 gm	-	-	-	-	-
4	Polyvinyl Alcohol	-	-	0.5 gm	-	-	-	-
5	Polyethylene	-	-	-	0.5 gm	-	-	-
6	Polypropylene	-	-	-	-	0.5 gm	-	-
7	Polyvinylpyrrolidone	-	-	-	-	-	0.5 gm	-
8	Polymethylmethacrylate	-	-	-	-	-	-	0.5 gm
9	PEG-400	6 ml	6 ml	6 ml	6 ml	6 ml	6 ml	6 ml
10	Dimethylsulphoxide	2 ml	2 ml	2 ml	2 ml	2 ml	2 ml	2 ml
11	Ethanol	Up to 20 ml	Up to 20 ml	Up to 20 ml	Up to 20 ml	Up to 20 ml	Up to 20 ml	Up to 20 ml

EVALUATION

Thickness of patch

At various spots along the transdermal film, the thickness is measured using a traveling microscope, dial gauge, screw gauge, or micrometer.

Drug content

In a shaker incubator, a precisely measured quantity of film (about 100 mg) is dissolved in 100 ml of a suitable solvent in which the medication is soluble. The solution is then agitated continuously for 24 hours. The whole solution is then sonicated after that. After filtering and sonication, the amount of medication in solution is determined spectrophotometric ally.

Percentage Moisture content

The produced films are weighed separately and maintained at room temperature in desiccators with calcium chloride for 24 hours. After a certain amount of time, the movies are weighed once again until they exhibit a steady weight. The difference between final and starting weight with regard to final weight is used to compute the % moisture content.

Percentage of moisture uptake

A weighted film was removed from a desiccator that had been held at room temperature for 24 hours and subjected to 84% relative humidity (a saturated solution of aluminum chloride) until the weight of the film remained constant. The difference between the final and original weights with regard to the beginning weight was used to compute the percentage of moisture absorption.

Tensile Strength

Polymeric films are placed between corked linear iron plates to measure their tensile strength. With the aid of an iron screen, one end of the films is maintained fixed, while the other end is attached to a freely moveable thread above a pulley. The dangling end of the thread is used to connect a pan with weights, which are increased gradually. The length of the film is measured using a pointer on the thread. It is noticed that the weight is exactly right to tear the film. The following equation may be used to determine the tensile strength; **Tensile strength= F/a.b (1+L/l)** F is the force required to break; a is width of film; b is thickness of film; L is length of film; l is elongation of film at break point.

Content uniformity test

10 patches are chosen, and each patch's material is chosen separately. Transdermal patches pass the test of content uniformity if 9 out of 10 patches have content that ranges from 85% to 115% of the given value, and 1 patch has content that ranges from 75% to 125% of the stated value. However, an extra 20 patches are tested for drug content if 3 patches test positive for substance in the 75% to 125% range. The transdermal patches pass the test if the range of these 20 patches is between 85% and 115%.

Uniformity of weight

By individually weighing 10 randomly chosen patches and figuring out the average weight, weight variation is explored. There shouldn't be a considerable difference between the individual weight and the average weight.

Folding Endurance

In order to evaluate folding endurance, it is necessary to ascertain the folding capacity of the films that are often folded under harsh circumstances. The test for folding endurance involves folding the film repeatedly until it breaks. Folding endurance value is the maximum number of folds a film can endure without breaking.

Flatness

A transdermal patch shouldn't contract over time and have a smooth surface. With the use of a flatness research, this may be shown. One strip is cut from the center and two from each side of patches to determine flatness. Each strip's length is measured, and the variance in length is quantified by calculating the percent constriction. 100% flatness is similar to 0% constriction.

% Constriction =L1 – L2/L1X 100

L2 = Final length of each strip

L1 = Initial length of each strip

Rolling ball test

In this test, the distance a stainless steel ball travels along an adhesive with an upward facing surface is measured. The adhesive's tackiness affects how far the ball will roll.

RESULT

Table 2: Resultive value of all formulations

Parameter	F1	F2	F3	F4	F5	F6	F7
Thickness (µm)	385±12	300±11	415±8	398±10	401±12	411±5	391±15
% Drug Content	97±1.2	99±0.2	96±1.1	98±1.3	98±0.8	96±1.3	97±0.8
% Moisture content	1.6±0.2	1.9±0.5	2±0.2	1.8±0.9	1.5±0.12	1.9±0.2	1.8±0.9
% Moisture uptake	2.5±0.5	2.6±0.7	2.4±0.3	2.5±0.2	2.4±0.3	2.9±0.1	2.6±0.2
Tensile Strength (dyne cm-2)	78.15±0.2	85.90±0.5	81.23±0.3	79.55±0.4	76.95±0.6	77.95±0.4	79.88±0.2
% Weight Uniformity	98±1.3	99±0.1	94±1.3	97±1.6	94±0.3	92±1.5	96±0.6
Folding Endurance	195±5	245±6	185±9	199±4	204±5	175±6	115±5
% Flatness	98±0.8	99±0.5	98±1.1	96±1.3	98±0.2	98±1.5	98±0.6
Rolling ball test (cm)	10	6	12	9	13	10	11

CONCLUSION

Drugs having a short elimination half-life of less than 3 hours and hepatic first pass metabolism are most suited for transdermal drug delivery devices. A transdermal patch containing aceclofenac was created using a mixture of HPMC and MC. Transdermal patches were being prepared using all the polymers, but HPMC K100 M was producing the greatest results. All of the transdermal patches' assessment parameters, according to the results, were satisfactorily provided by the F2 formulation. Thus, it was determined that HPMC K100M was the ideal polymer to employ in the preparation of transdermal patches.

REFRENECE

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