Original Article

FUTURE JOURNAL OF PHARMACEUTICALS AND HEALTH SCIENCES

Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/fjphs

Formulate and evaluate transdermal patches using Econazole

Archana B*[1], Konda Sri Chaya Reddy[1], Gadapati Amulya Shreshta[1], Abubakar Sadiq[2]

[1]Bojjam Narasimhulu Pharmacy College for Women, 17-1-383, Vinay Nagar campus, Saidabad, Hyderabad – 500059, Telangana, India

[2]St Mary's group of institutions, Deshmukh (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist), Hyderabad – 508284, Telangana, India

Article History:

Received on: 17 Mar 2024
Revised on: 28 Apr 2024
Accepted on: 30 Apr 2024

Keywords:

Econazole,
Transdermal Patches,
HPMC,
Eudragit

Abstract

The current project aims to formulate and evaluate econazole-based transdermal patches. At present, the market offers econazole tablets for purchase. These dose formulations do not elicit cooperation from patients. Therefore, because transdermal drug administration systems are simple to use and improve patient compliance, they have begun to gain momentum as innovative drug delivery methods. The research aims to use polymers like HPMC K 15M, HPMC K 100M, and HPMC K200M to build and evaluate econazole transdermal patches. The solvent casting technique for making econazole transdermal patches. To determine the formulation's approximate drug content, an appropriate in vitro technique is employed to investigate the drug release pattern. To delay the drug's release over a long period. To develop a dose form that prevents patient compliance and reduces dosage frequency for optimal drug utilization. Tween 80 plasticizer concentration was essential for patch creation and separation characteristics. For use as a plasticizer and solubility enhancer during the shelf life term, Tween 80 is chosen. The formulation F-5 was optimized for the desired qualities and was an effective batch.

∗Corresponding Author
Name: Archana B
Phone: +91 7416367155
Email: archanabiradar07.abab@gmail.com

eISSN: 2583-116X
DOI: https://doi.org/10.26452/fjphs.v4i2.608

Production and hosted by
Pharmasprings.com

INTRODUCTION

A transdermal patch is an adhesive patch that has been medicated and is applied to the skin to allow a prescribed drug dosage to pass through the skin and enter the bloodstream. A transdermal drug delivery route has an advantage over other forms of delivery of drugs (oral, topical, intravenous, or intramuscular). The drug is released into the patient's body controlled through the patch, typically via a porous membrane covering a reservoir of drugs or by the body's heat-melting thin layers of drugs embedded in the adhesive [1]. Researchers have developed microneedle transdermal patches (MNPs) to get around the skin's restriction. MNPs are made up of various microneedles and enable a wider range of compounds or molecules to be passed through the skin without needing to micronize the drug beforehand. A transdermal patch called a microneedle patch (MNP) minimizes the

Table 1 Composition of different gel formulations

Formulation Code	Drug (gram)	Polymer (gram)	Ethanol ml	Enhancers		Water q.s. to 100 ml
				Almond oil (g)	Tween80 (g)	
F1	2	1	10	-	-	100
F2	2	1	10	1	-	100
F3	2	1	10	2	-	100
F4	2	1	10	3	-	100
F5	2	1	10	-	0.1	100
F6	2	1	10	-	0.3	100
F7	2	1	10	-	0.3	100
F8	2	1	10	2	0.4	100
F9	2	1	10	2	0.5	100

Table 2 Formulation of econazole Transdermal patches

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Econazole	15	15	15	15	15	15	15	15	15
HPMC K15M	35	35	35	-	-	-	-	-	-
HPMC K100M	-	-	-	40	40	40	-	-	-
HPMC K200M	-	-	-	-	-	-	40	40	40
PVP K30	15	35	55	15	35	55	15	35	55
Tween-80	15	15	15	15	15	15	15	15	15
sorbitol	60	40	20	60	40	20	60	40	20

drawbacks of traditional transdermal patches while maintaining their benefits. MNPs can readily pass through the stratum corneum, a 20 µm-thick layer of skin tissue that allows macromolecules up to that size. They can embed up to 102–104 needles per square cm of patch and be coated or encapsulated with the targeted medicine [2].

Regarding delivery, MNPs are more effective than topical or oral consumption. Researchers aim to obtain faster peak concentrations (Cmax) in MNPs in drug delivery studies than alternative approaches. According to the study, oral consumption takes an hour to reach peak concentration, whereas MNPs can achieve peak concentration as quickly as 20 minutes (Tmax). In addition, compared to oral consumption, the Cmax from MNPs might be up to six times higher [3]. Enabling quick delivery so that the body receives the maximum amount of the prescribed drug. The MNPs may be an alternative to achieve approximately the same time and concentration in cases of skin injuries and needle anxiety.

Materials and Methods:

Six criteria to evaluate different ethanol and acetone ratios and different grades of eudragit and ethyl cellulose: viscosity, drying time, stickiness, look and integrity on the skin, and water washability. The study employed propylene glycol (PG) and polyethylene glycol 400 (PEG 400) as plasticizers and solubilizers. The antifungal efficacy research, leak test, pH, drug content, evaporation time, average weight per dosage, spray angle, spray pattern, and in vitro drug release were all assessed for the TS.

After weeks of investigating drug-excipient compatibility utilizing the following excipients, they were selected for the formulation.

METHODOLOGY

Compatibility Study:

Fourier transform infrared radiation:

Infrared absorption spectra of pure drug, pure polymer, and a physical combination of drug and polymer were measured using the KBr pellet method for polymer-drug interaction studies ranging from 4000 cm-1 to 400 cm-1 [4].

Formulaton of Econazole transdermal patches:

Procedure:

Glipiside transdermal patches were made using the solvent casting technique. Mix equal parts DCM and ethanol, then dissolve the drugs first [5].

Table 3 Stability Storage Conditions

Stability Storage Category	The testing schedule for Physical and Chemical attributes
LONG TERM 25°C ± 2°C / 60% ± 5% RH	3, 6, 9, 12, 18, 24 and annually till expiry and 6 Months hence after.
ACCELERATED 40°C ± 2°C / 75% ± 5% RH	1, 2, 3 & 6 Months
INTERMEDIATE 30°C ± 2°C / 60% ± 5% RH	3, 6, 9 & 12 Months
ZONE IV 30°C ± 2°C / 70% ± 5% RH	3, 6, 9, 12, 18, 24 and annually till expiry and 6 Months hence after.

Table 4 Evaluation criteria for transdermal econazole patches

Formulation code	Thickness	Weight variation	Drug content	Folding endurance	Tensile strength
F1	174	Pass	98.21	204	2.75
F2	162	Pass	99.16	195	2.95
F3	155	Pass	99.65	215	3.13
F4	163	Pass	98.85	212	3.05
F5	159	Pass	99.39	214	2.84
F6	154	Pass	99.97	208	2.95
F7	142	Pass	99.69	219	3.17
F8	135	Pass	99.81	233	2.88
F9	152	Pass	99.33	208	2.48

Next, add each ingredient one at a time, stirring constantly to ensure adequate dissolution.

The solutions were poured onto a 9-cm-diameter glass petri dish and baked at 70°C to generate a peelable coating. After that, the dried films were divided into rectangular pieces with a total surface area of 4.0 cm2 (2.0 cm × 2.0 cm) [6]. The desired dosage of Glipiside was 10 mg per 4.0 cm2 film.

Evaluation of Transdermal Patches:

1. Thickness
2. Weight variation
3. Drug content
4. Folding endurance
5. Tensile strength
6. In-vitro drug release

Thickness: A micrometer was used to measure the thickness of the patches at three distinct locations, and mean values were calculated [7].

Weight Variation: Weighing each patch separately after being selected randomly allowed us to vary the patches' mass. These calculations for every formulation.

Drug Content: Dichloromethane was dissolved in 5 mL of phosphate buffer pH 7.4 to make a volume of 10 mL after patches with a specific area (1 cm2) were dissolved in it. The dichloromethane was removed using a rotary vacuum evaporator at 45 °C. Identically treated drug-free patch was used to create a blank. After passing through a 0.45 µm membrane filter and being appropriately diluted, the solutions were measured for absorbance at 274 nm using a double-beam UV-Vis spectrophotometer [8].

Folding Endurance:

This was ascertained by folding a single film repeatedly at the same spot until it broke. The folding endurance of a film is measured by the number of times in the same direction without cracking or breaking.

Tensile Strength:

A pulley system was used to pull the polymeric patch to measure its elongation as a tensile strength. Weights were added to the pan gradually to increase the pulling force until the patch broke.

On the graph paper, a magnifying lens was used to measure the elongation, or the distance the pointer moved before breaking. Tensile strength was computed as kg cm [9].

In-vitro skin permeation studies:

Studies on in vitro penetration through the skin were conducted using a Franz diffusion cell with a 22.5 mL receptor compartment capacity. The donor and receptor compartments of the diffusion cell were positioned between the excised rat's abdomen skin (Wistar albino). After applying the prepared patches to the skin, paraffin film was used. A phosphate buffer with pH 7.4 was put within the diffusion cell's receptor compartment. The entire assembly was secured to a magnetic stirrer, and magnetic beads were used to continually swirl the solution in the receptor compartment at 50 revolutions per minute. The temperature was kept at 32 ± 0.5 °C. The samples were taken out at various intervals and subjected to spectrophotometric analysis to determine the drug content. After every sample removal, the receptor phase was refilled with the same volume of phosphate buffer (pH 7.4). Plotting the cumulative percentages of drugs infused per square centimeter of the patches against time was carried out [10].

STABILITY STUDIES[11]

The intrinsic stability of the drug material, knowledge of the appropriate excipients to employ and how to combine them with the drug for maximum effectiveness, and assurance that no harmful substances will form are all essential considerations when building a dosage form. Therefore, reasonable definitions of acceptable limits and compromises are required. They can be costly and time-consuming because long-term stability studies must confirm these data and calculate the final dosage form's shelf life or expiration date.

As a result, identifying the research designs and setups with the highest chance of success is imperative. Therefore, identifying and assisting in avoiding or controlling situations where the stability of the active ingredient may be affected is the goal of stability research.

Rationale for stability studies [11]:

The amount of therapeutic agents in the dosage form may significantly decrease due to the active drug degrading chemically.

Even if the active drug's chemical breakdown might not be costly, the process could result in the formation of a hazardous byproduct.

A pharmacological product's instability may cause the dosage form's therapeutic efficacy to decline significantly.

RESULTS AND DISCUSSION

Compatibility study:

FT-IR Study:

The drug's compatibility with the polymer was assessed by comparing the optimal formulation and standard drug using FTIR measurement.

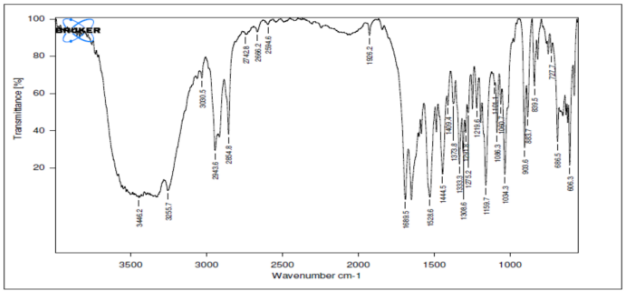

Figure 1: FTIR graph of econazole pure drug

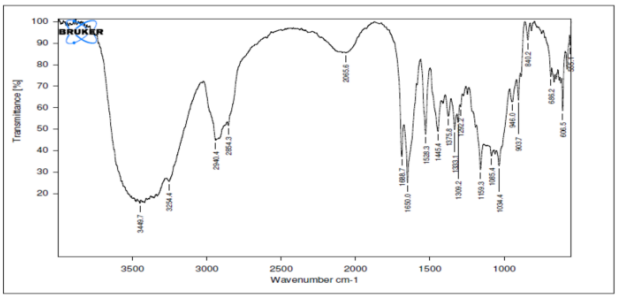

Figure 2: FTIR graph of econazole best formulation

STABILITY STUDIES:

The chosen formulation, F5, was kept for three months at 40°C ± 2°C / 75% ± 5% RH. Samples were analyzed after 1, 2, and 3 months of storage.

SUMMARY AND CONCLUSION:

It has been concluded that Econazole transdermal patches were successfully prepared with HPMC K15M, HPMC K100M, and HPMC K 200M. The quantity of plasticizer Tween 80 was crucial to patch creation and separation qualities. Tween 80

Table 5 Transdermal patches: *in vitro* drug release profile

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	28	29	22	22	17	6	13	4	0
2	42	41	32	39	25	9	21	12	4
3	55	51	52	58	37	16	27	18	8
4	62	55	53	65	54	21	43	32	18
6	84	73	65	75	65	28	55	43	29
8	92	85	79	82	79	47	61	56	44
10	100	92	83	99	87	55	72	68	52
12	100	100	97	100	99	72	79	72	64

Table 6 In-vitro F5 release profile during stability testing (40°C ± 2°C / 75% ± 5% RH)

Time (Hrs)	Initial	Month 1	Month 2
1	17	14	17
2	23	23	24
3	35	34	37
4	54	54	52
6	63	63	63
8	79	76	75
10	85	83	84
12	99	98	97

is chosen as a solubility enhancer and plasticizer during the shelf life period. The F-5 is considered suitable and has been optimized for desirable qualities.

ACKNOWLEDGEMENT

I want to thank the principal and management of St mary's group of institutions, Deshmukh (village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist), Hyderabad, for their constant support and guidance in completing this research work.

Funding Support: The Author declares that there is no funding.

Conflict of Interest: The Author declares that there is no conflict of interest.

REFERENCES

[1] N.Harper Bellantone, S. Rim ∗, M.L. Francoeur, and B. Rasadi. Enhanced percutaneous absorption via Iontophoresis I. Evaluation of an in-vitro system & transport of model compound. International Journal of Pharmaceutics, 30(1):63-72, 1986.

[2] H S Nelson. Beta-adrenergic bronchodilator. England Journal of Medicine, 333(8):499-506, 1995.

[3] Mark R. Prausnitz and Robert Langer. Transdermal drug delivery. Nature Biotechnology, 26(11): 1261–1268, 2008.

[4] P W Wertz, D C Swartzendruber, K C Madison, and D T Downing. The composition & morphology of Epidermal cyst lipids. The Journal of Investigative Dermatology, 89(4): 417-425, 1987.

[5] Eliana B. Souto, Joana F. Fangueiro, Ana R. Fernandes, Amanda Cano, Elena Sanchez-Lopez, Maria L. Garcia, Patrícia Severino, Maria O. Paganelli, Marco V. Chaud, and Amelia M. Silva. Physicochemical and biopharmaceutical aspects influencing skin permeation and role of SLN and NLC for skin drug delivery. Heliyon, 8(2): e08938, 2022.

[6] J Hadgraft, and W J Pugh. The selection and design of topical and transdermal agents: a review. The Journal of Investigative Dermatology: Symposium Proceedings, 3(2): 131-135, 1998.

[7] D.I.J. Morrow, P.A. McCarron, A.D. Woolfson, and R.F. Donnelly. Innovative Strategies for enhancing topical and transdermal drug delivery. The Open Drug Delivery Journal, 1, 36-59, 2014.

[8] Michael N Pastore, Yogeshvar N Kalia, Michael Horstmann, and Michael S Roberts.

Transdermal patches: history, development and pharmacology. British Journal of Pharmacology, 172(9):2179-209, 2015.

[9] Othman A Al Hanbali, Haji Muhammad Shoaib Khan, Muhammad Sarfraz, Mosab Arafat, Shakeel Ijaz, and Abdul Hameed. Transdermal patches: Design and current approaches to painless drug delivery. Acta Pharmaceutica, 69(2):197-215, 2019.

[10] Farzaneh Sabbagh, and Beom Soo Kim. Recent advances in polymeric transdermal drug delivery systems. Journal of Controlled Release, 341:132-146, 2022.

[11] Purnendu Kumar Sharma, Apoorva Panda, Adwait Pradhan, Jiaxiang Zhang, Ruchi Thakkar, Chang-Hee Whang, Michael A Repka, and S Narasimha Murthy. Solid-State Stability Issues of Drugs in Transdermal Patch Formulations. AAPS PharmSciTech, 19(1):27-35, 2018.

[12] Johannes Wohlrab, B Kreft, and B Tamke. Skin tolerability of transdermal patches. Expert Opinion on Drug Delivery, 8(7):939-948, 2011.