International Journal of Enhanced Research in Medicines & Dental Care (IJERMDC),
ISSN: 2349-1590, Vol. 13 Issue 10, October 2026

Formulation and Evaluation of Quercetin-Loaded Transdermal Patches by Solvent Casting Method

C. Priya Dhaarani*[1], Dr. M. Rajesh[2], S.V.S. Harish[1]

[1]M. Pharm Student, Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi. (Affiliated to the The TN DR. M.G.R Medical University, Chennai)
[2]Professor and Head, Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi. (Affiliated to the The TN DR. M.G.R Medical University, Chennai)

Corresponding Author Details**:** C. Priya Dhaarani, Email: chandranpriya08@gmail.com

ABSTRACT

The present study aimed to formulate and evaluate Quercetin-loaded transdermal patches using Hydroxypropyl Methylcellulose (HPMC) and Ethyl Cellulose (EC) as polymers by the solvent casting method, with PEG 400 as a plasticizer. Preformulation studies, including organoleptic properties, solubility, melting point and drug-excipient compatibility studies by FT-IR, were performed. Different formulations were prepared and evaluated for physical appearance, weight variation, thickness, folding endurance, surface pH, moisture absorption, moisture loss, drug content and *in vitro* drug diffusion studies. The prepared patches exhibited satisfactory physical appearance, uniformity and flexibility, with thickness ranging from 0.011 ± 0.002 to 0.022 ± 0.003 mm, folding endurance ranging from 74 ± 2 to 112 ± 3 folds and surface pH ranging from 5.4 ± 0.1 to 6.3 ± 0.1. The drug content ranged from 36.05% to 90.05%, while cumulative drug release at 12 hours ranged from 78.08% to 98.21%. Formulation F6 was selected as the optimized formulation based on its higher drug content (90.05%) and cumulative drug release (95.78%), providing a suitable balance between drug incorporation and drug release. SEM analysis of formulation F6 revealed a relatively smooth, compact and uniform surface without major structural defects. Stability studies conducted for formulation F6 at 40 ± 2 ^{0}C/75 ± 5% RH for one month showed no significant changes in drug content or *in vitro* drug release. Overall, the study demonstrated the successful development of Quercetin-loaded transdermal patches with formulation F6 identified as the optimized formulation based on its satisfactory physicochemical characteristics, sustained drug release, acceptable surface morphology and short-term stability, demonstrating its potential as a controlled transdermal delivery system for Quercetin.

Key Words: Ethylcellulose, Hydroxypropyl Methylcellulose, Polyethylene Glycol 400, Quercetin, Solvent casting and Transdermal patch.

INTRODUCTION

Transdermal drug delivery systems (TDDS) are advanced pharmaceutical dosage forms designed to deliver therapeutic agents through the skin into the systemic circulation. These systems provide an alternative route of drug administration by overcoming certain limitations associated with conventional oral dosage forms. Transdermal drug delivery involves the controlled transport of drugs across the skin, particularly through the stratum corneum, which acts as the primary barrier to drug permeation. The drug is subsequently absorbed into the systemic circulation, producing the desired therapeutic effect. The outermost layer of the epidermis, known as the stratum corneum, plays a significant role in regulating the permeation of drugs through the skin. Although this barrier protects the body, it also limits the penetration of many therapeutic agents. Therefore, the development of suitable drug delivery systems is essential for improving drug permeation and achieving effective therapeutic concentrations. Transdermal drug delivery offers several advantages over conventional routes of administration[1]. It can bypass the gastrointestinal tract and reduce the effect of hepatic first-pass metabolism, it may improve drug bioavailability, maintain relatively consistent plasma drug concentrations, reduce fluctuations in drug levels and decrease the frequency of administration. Furthermore, transdermal patches are non-invasive, convenient and may improve patient compliance. They can also be removed easily when necessary, providing an additional advantage over certain other drug delivery systems[2].

The selection of an appropriate drug candidate, polymers, plasticizers and formulation method is essential for the successful development of a transdermal patch[3]. The objective of this study is to formulate and evaluate quercetin-

loaded transdermal patches using Hydroxypropyl Methylcellulose (HPMC) and Ethylcellulose (EC) as polymeric matrices by the solvent-casting method. The developed transdermal patches are intended to provide sustained and controlled release of quercetin, thereby maintaining consistent drug levels in the body over an extended period. This approach may reduce the frequency of dosing, minimize fluctuations in drug concentration and potentially improve patient compliance[4].

MATERIALS AND METHODS

Quercetin was procured from Aurochem Laboratories, Mumbai. Hydroxypropyl Methylcellulose and Ethylcellulose were procured from Yarrow Chem Products, Mumbai. PEG 400 was procured from Larkchem Pvt. Ltd., Mumbai. Ethanol was procured from Rankem Chemicals Pvt. Ltd., Haryana. All other chemicals and reagents used in the formulation and evaluation were of analytical grade.

METHODS:

PREFORMULATION STUDIES:

❖ ORGANOLEPTIC PROPERTIES:

The Quercetin sample was examined visually for its physical characteristics such as appearance, colour and odour[5].

❖ SOLUBILITY ANALYSIS:

The solubility of Quercetin was studied in selected solvents such as water, ethanol and pH 6.8 phosphate buffer. A small quantity of the drug was added to each solvent and mixed thoroughly. The solubility was assessed based on the amount of drug dissolved in the respective solvent[6].

❖ MELTING POINT DETERMINATION:

The melting point of Quercetin was determined by the capillary tube method. A small quantity of finely powdered drug was filled into a capillary tube and placed in a melting point apparatus. The temperature was gradually increased and the temperature at which the drug melted was noted[7].

❖ FT-IR SPECTRAL STUDIES:

FT-IR analysis was performed to identify the characteristic functional groups of Quercetin and to assess possible interactions between the drug and excipients. The drug, individual excipients and their combination were subjected to FT-IR analysis. The obtained spectra were compared with the characteristic peaks of Quercetin to determine the compatibility of the formulation components[8].

FORMULATION OF QUERCETIN TRANSDERMAL PATCHES BY SOLVENT CASTING METHOD:

The solvent casting method was used for the preparation of Quercetin transdermal patches. The required quantities of Hydroxypropyl Methylcellulose and Ethylcellulose were accurately weighed and dissolved separately in suitable solvents. Quercetin was dissolved/dispersed in ethanol and added gradually to the polymeric solution with continuous stirring. PEG 400 was incorporated as a plasticizer and the mixture was stirred thoroughly to obtain a homogeneous solution. The prepared polymeric solution was kept aside to remove entrapped air bubbles. The homogeneous solution was then poured into a suitable Teflon/glass mould and allowed to dry at controlled temperature until a uniform film was formed. The dried film was carefully removed from the mould and cut into the required size. The prepared Quercetin transdermal patches were stored in a desiccator until further evaluation[9]. The composition of Quercetin transdermal patches was shown in Table-1.

Table 1: Formulation of Quercetin Transdermal Patches

		FORMULATION CODE							
S.NO	**INGREDIENTS**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
1.	Quercetin(mg)	20	20	20	20	20	20	20	20
2.	Hydroxypropyl Methylcellulose(g)	1.5	1	1	1	1.5	1	1.5	1.5
3.	Ethylcellulose(g)	1	1	1	1.5	1	1.5	1.5	1.5
4.	PEG 400 (mL)	0.3	0.5	0.3	0.3	0.5	0.5	0.3	0.5
5.	Ethanol (mL)	5	5	5	5	5	5	5	5
6.	Purified Water(mL)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

EVALUATION OF QUERCETIN TRANSDERMAL PATCHES:

❖ PHYSICAL APPEARANCE:

The prepared patches are visually inspected for color, transparency, smoothness, flexibility, uniformity and the absence of air bubbles or surface imperfections. A uniform and defect free patch indicates good formulation quality[10].

❖ **THICKNESS:**

Patch thickness is measured at different locations using a digital micrometer or vernier caliper and the average thickness was recorded. Uniform thickness is essential for consistent drug loading and controlled drug release[11].

❖ **WEIGHT VARIATION TEST:**

Weight variation was determined by weighing ten patches individually from each batch on an electronic balance and average weight was calculated. The individual weight should not deviate significantly from the average weight[12].

❖ **FOLDING ENDURANCE:**

Folding endurance is determined by repeatedly folding the patch at the same point until it breaks. This test evaluates the flexibility and mechanical strength of the patch. A higher folding endurance value indicates better durability during handling and application. This test is repeated three times for reproducibility[13].

❖ **DETERMINATION OF pH:**

Place a small section of the patch in a clean dry container and add about 5 mL of pH 6.8 phosphate buffer. Allow the patch to soak in the liquid for a specified time usually five minutes to allow for the transfer of the patch's pH to the liquid. Next, immerse the pH meter electrode into the liquid covering the patch ensuring that it is fully submerged. Record the pH value displayed on the pH meter. Take multiple readings at different locations on the patch to ensure consistency[14].

❖ **DRUG CONTENT ANALYSIS:**

The patches (2cm × 2 cm) were dissolved in 100ml of pH 6.8 phosphate buffer. The contents were stirred using a magnetic bead to dissolve the patches. After suitable dilution, the resultant solution was filtered through 0.45µm Whatman filter paper and the drug content was determined at 370nm against pH 6.8 phosphate buffer as blank using a UV-Visible spectrophotometer[15].

❖ **MOISTURE ABSORPTION STUDIES:**

Weighed flims are held at room temperature in a desiccator with a saturated solution of aluminium chloride of 100ml, which preserves relative humidity at 79.5%. These films are then withdrawn and weighed after three days. The moisture absorption percentage was determined using the following formula[16].

$$\% \text{ moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{Final\,weight} \times 100$$

❖ **MOISTURE LOSS STUDIES:**

The prepared films are individually weighed and stored at room temperature for 24 hours in a desiccator that contains calcium chloride. After 72 hours, the patches were removed and weighed accurately. Percentage of moisture loss was calculated by using the following formula[17].

$$\% \text{ moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{Initial\,weight} \times 100$$

❖ ***IN VITRO* DIFFUSION STUDIES:**

The drug release study is performed using a Franz diffusion cell. The transdermal patch (2 cm × 2 cm) is placed on a dialysis membrane that separates the donor and receptor compartments. The receptor compartment is filled with phosphate buffer (pH 6.8) which is continuously stirred and maintained at 37 ± 0.5°C using a hotplate magnetic stirrer with magnetic beads to simulate physiological conditions. At predetermined time intervals (1, 2, 3,4…… upto 12 hours), a fixed volume of the receptor medium is withdrawn and replaced with an equal volume of fresh medium to maintain sink conditions. The collected samples after suitable dilution are analyzed at 370nm using UV–Visible spectrophotometry to determine the amount of quercetin released[18].

❖ **SCANNING ELECTRON MICROSCOPY:**

The surface morphology of the best Quercetin transdermal patch was examined using Scanning Electron Microscopy (SEM). A small piece of the patch was cut and mounted on an aluminium stub using double-sided adhesive tape. The sample was coated with a thin layer of conductive material and examined under a scanning electron microscope at suitable magnification. The SEM images were captured to evaluate the surface morphology, uniformity, porosity and distribution of the drug within the polymeric matrix. The obtained images were used to assess the surface characteristics of the prepared Quercetin transdermal patch[19].

❖ **STABILITY STUDY:**

Stability study for the best formulation of Quercetin (short term study) was performed at 40 ± 2°C /75% ± 5% RH for 1 month. Samples were analyzed for drug content and *in vitro* diffusion studies, during initial period and at an intervals of

15 and 30 days[20].

RESULTS AND DISCUSSION

GENERAL APPEARANCE:

The general appearance of all formulated patches was examined. The patches were found to be smooth, uniform and flexible with pale yellow colour. No significant cracks, pores, drug crystals were observed on the surface of the patches.

❖ **EVALUATION OF QUERCETIN TRANSDERMAL PATCHES:**

The prepared patches were evaluated for various parameters. The results are mentioned in Table 2. The thickness of the prepared transdermal patches ranged from 0.011 ± 0.002mm to 0.022 ± 0.003 mm. The slight variation in thickness among the formulations indicates reasonably uniform patch formation and polymer distribution of the patches. The weight variation of the prepared patches ranged from 0.88 ± 0.02 to 1.45mg ± 0.03 mg. The highest weight was observed in formulation F5 (1.45 ± 0.03 mg), whereas the lowest weight was observed in F7 (0.88 ± 0.02 mg). The folding endurance values of the prepared patches ranged from 74 ± 2 to 112 ± 3 folds. Formulation F7 showed the highest folding endurance (112±3 folds), indicating better flexibility and mechanical strength, whereas F8 showed lowest value (74±2 folds). The results revealed that the prepared patches possessed good mechanical strength. The surface pH of the formulated transdermal patches ranged from 5.4 ± 0.1 to 6.3 ± 0.1. These pH values were close to the physiological pH of the skin and hence considered suitable for transdermal application, thereby minimizing the possibility of skin irritation.

Table 2: Physicochemical Evaluation Parameters of Quercetin Transdermal Patches

FORMULATION CODE	THICKNESS (mm)	WEIGHT VARIATION (mg)	FOLDING ENDURANCE	pH
F1	0.019±0.002	1.06±0.02	75±1	5.4±0.1
F2	0.022±0.003	1.01±0.03	83±1	5.7±0.2
F3	0.017±0.001	1.20±0.03	79±2	6.1±0.1
F4	0.011±0.002	0.92±0.02	97±1	5.6±0.2
F5	0.021±0.003	1.45±0.03	80±2	6.2±0.1
F6	0.018±0.002	1.00±0.01	86±1	5.9±0.2
F7	0.016±0.001	0.88±0.02	112±3	6.3±0.1
F8	0.020±0.003	1.10±0.03	74±2	6.0±0.2

***All the values are expressed as mean ± SD, n=3**

❖ **DRUG CONTENT AND MOISTURE RELATED PARAMETERS:**

The percentage moisture absorption, moisture loss and percentage drug content are shown in the table-3.The percentage moisture absorption ranged from 2.30 ± 0.01% to 4.04 ± 0.04%, with formulation F4 showing the highest moisture absorption (4.04 ± 0.04%) and F7 showing the lowest (2.30 ± 0.01%). The percentage moisture loss ranged from 2.31 ± 0.01% to 3.64 ± 0.02%, with the lowest value observed for formulation F1 (2.31 ± 0.01%) and the highest for F8 (3.64 ± 0.02%). Overall, the results indicate that the prepared transdermal patches exhibited satisfactory moisture handling properties. The percentage drug content of the prepared Quercetin transdermal patches was found to be in the range of 36.05±0.63 to 90.05±0.58 for all the formulations. Among the formulations, F6 showed the highest drug content of 90.05%, whereas F5 showed the lowest drug content of 36.05%. Among the formulations, F6 demonstrated the highest drug content (90.05%) along with relatively low moisture absorption (2.91%) and moisture loss (3%) indicating better overall physical characteristics.

Table 3: Evaluation Parameters of Quercetin Transdermal Patches

FORMULATION CODE	PERCENTAGE MOISTURE ABSORPTION (%)	PERCENTAGE MOISTURE LOSS (%)	PERCENTAGE DRUG CONTENT (%)
F1	2.99±0.02	2.31±0.01	87.00±0.52
F2	3.81±0.03	2.97±0.02	85.00±0.61
F3	2.44±0.01	2.50±0.03	39.05±0.48
F4	4.04±0.04	3.16±0.01	83.05±0.55
F5	2.60±0.01	2.67±0.02	36.05±0.63
F6	2.91±0.02	3.00±0.01	90.05±0.58
F7	2.30±0.01	3.53±0.03	86.05±0.67
F8	3.51±0.02	3.64±0.02	84.00±0.56

***All the values are expressed as mean ± SD, n=3**

❖ ***IN VITRO* DIFFUSION STUDIES:**

The results of *in vitro* drug release data of the prepared patches are shown in the table-4 and *in vitro* drug release profiles are shown in figure-1. The percentage drug release of Quercetin transdermal patches ranges from 78.08% to 98.21% at the end of 12 hours. Formulations F3 and F5 exhibited drug release of 91.77% and 78.08% respectively, but they showed considerably lower drug contents of 39.05% and 36.05%, respectively, indicating inadequate drug incorporation and making them unsuitable as optimized formulations. Formulations F4 and F7 exhibited comparatively lower cumulative drug release of 82.51% and 86.36% respectively compared to Formulations F1, F2, F6 and F8. Formulations F1 and F2 has better drug release (92.98% & 91.18%) but comparatively less than formulations F6 and F8 (95.78% and 98.21%) making them unsuitable as optimized formulations.

Formulations F6 and F8 showed drug contents of 90.05% and 84%, respectively. When comparing the drug content and drug release of formulations F6 and F8, the drug content of formulation F6 is 6.5% points higher than F8 and drug release is only 2.43% points lower than F8. Although formulation F8 exhibited the maximum cumulative drug release of 98.21%, its drug content was comparatively lower (84.0%) and lowest folding endurance value (74). A transdermal patch should possess adequate drug incorporation together with an appropriate and controlled drug release profile. Therefore, the formulation providing a suitable balance between drug content and drug release was considered preferable. Formulation F6 exhibited the highest drug content (90.05%) among the investigated formulations and demonstrated a high cumulative drug release of 95.78% which demonstrates a particularly good balance between drug incorporation and drug release performance.

Table 4: *In vitro* Drug Release Data of Quercetin Transdermal Patches

S.NO	TIME IN MINS.	PERCENTAGE DRUG RELEASE (%)							
		FORMULATION CODE							
		F1	F2	F3	F4	F5	F6	F7	F8
1.	1	32.07±0.52	22.59±0.45	35.18±0.52	32.46±0.54	27.12±0.47	23.90±0.43	23.24±0.46	25.48±0.44
2.	2	38.09±0.61	34.59±0.53	44.05±0.58	37.84±0.58	40.00±0.55	39.15±0.52	33.18±0.54	34.40±0.53
3.	3	45.05±0.48	41.88±0.49	52.27±0.63	39.28±0.49	40.82±0.51	41.59±0.48	37.34±0.50	36.55±0.49
4.	4	51.02±0.55	48.59±0.57	54.30±0.55	45.15±0.56	46.30±0.59	46.83±0.55	42.08C0.57	41.31±0.56
5.	5	57.12±0.63	55.29±0.62	55.94±0.61	50.78±0.61	56.16±0.64	51.71±0.60	46.59±0.62	45.71±0.61
6.	6	63.10±0.58	61.41±0.56	61.64±0.66	56.17±0.57	57.80±0.58	56.34±0.57	50.75±0.56	49.88±0.55
7.	7	68.73±0.67	67.18±0.65	66.83±0.70	61.08±0.63	61.91±0.66	60.73±0.64	54.68±0.64	53.81±0.63
8.	8	74.36±0.72	72.71±0.69	70.25±0.64	65.75±0.68	63.01±0.70	64.88±0.69	58.50±0.68	57.62±0.69
9.	9	79.54±0.64	77.76±0.73	72.15±0.69	70.06±0.71	69.58±0.74	68.66±0.72	61.97±0.73	61.07±0.72
10.	10	83.67±0.59	82.59±0.68	78.22±0.73	74.13±0.65	71.78±0.68	72.20±0.67	65.20±0.66	67.62±0.67
11.	11	84.82±0.71	84.24±0.79	82.78±0.76	77.72±0.73	73.97±0.75	75.49±0.74	68.32±0.75	68.57±0.74
12.	12	92.98±0.76	91.18±079	91.77±0.81	82.51±0.78	78.08±0.80	95.78±0.82	86.36±0.81	98.21±0.83

***All the values are expressed as mean ± SD, n=3**

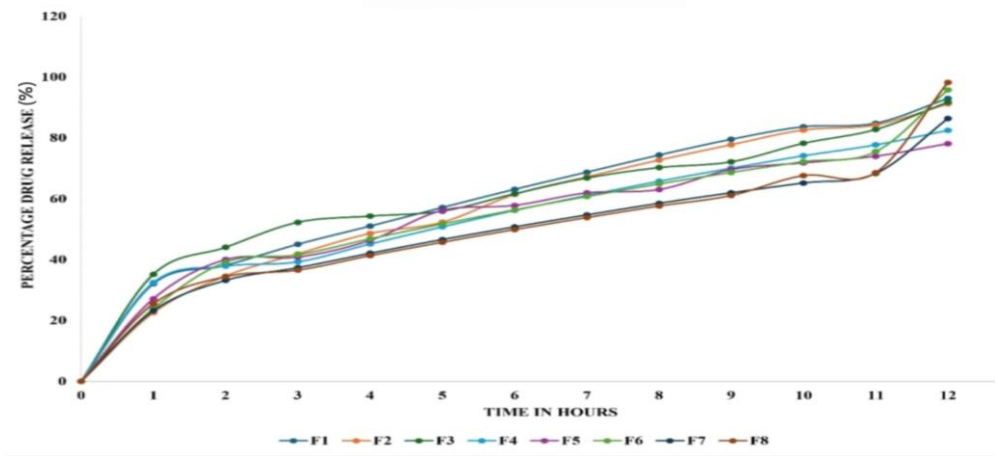


Fig 1: Drug Release Profiles of Quercetin Transdermal Patches

SCANNING ELECTRON MICROSCOPY ANALYSIS OF QUERCETIN TRANSDERMAL PATCH (F6):

The SEM analysis confirmed the successful formation of a uniform and stable quercetin transdermal patch. The surface morphology of the patch was found to be smooth and compact with fine textural features, indicating a homogeneous distribution of Quercetin within the Ethyl cellulose and Hydroxypropyl Methylcellulose polymer matrix. The absence of visible cracks and major defects suggests good compatibility between the drug and polymers and effective film forming ability of the formulation. The addition of PEG as plasticizer may have contributed to the flexibility and smoothness of the prepared patch. The SEM image of Quercetin trandermal patch at 1000x and 5000x magnification were shown in figure 2 and 3 respectively.

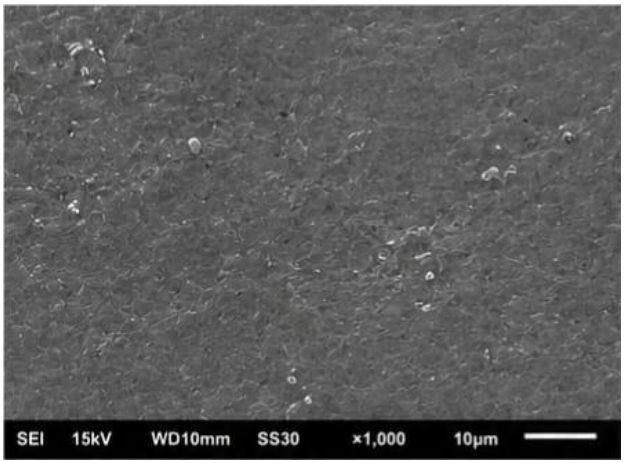
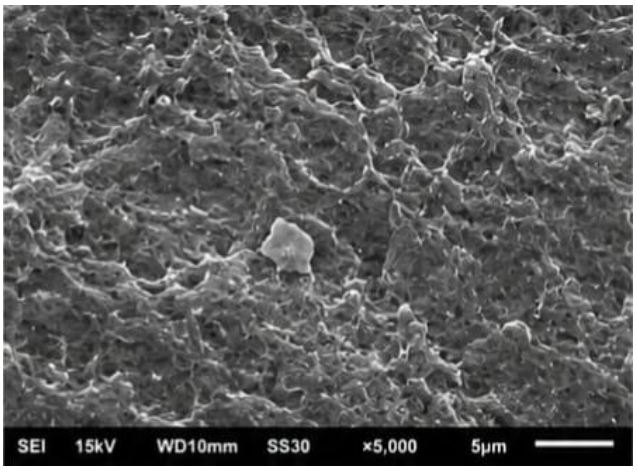


Fig 2: SEM Image of Quercetin Transdermal Patch (Formulation F6) (1000 X magnification)



3: SEM Image of Quercetin Transdermal Patch (Formulation F6) (5000 X magnification)

❖ **STABILITY STUDY:**

The optimized formulation F6 was selected for the stability study. The formulation was stored at 40 ± 2°C / 75 ± 5% RH for a period of 1 month. The stability study of the optimized formulation (F6) showed no significant changes in the drug content and *in vitro* drug release even after storage at 40 ± 2°C / 75 ± 5% RH for one month. Hence, the optimized formulation of Quercetin transdermal patch was found to be stable under the specified storage conditions. The results are presented in table-5.

Table 5: Stability Study Data of Optimized Formulation F6

S.NO	PARAMETERS	STORAGE CONDITIONS:40±2^{O}C/75%±5%RH		
		INITIAL PERIOD	15 DAYS	30 DAYS
1.	Drug content (%)	89.98±0.19	89.93±0.22	89.57±0.18
2.	*In vitro* drug release at the end of 12 hours (%)	95.73±0.22	95.71±0.21	95.46±0.19

CONCLUSION

Overall, the study demonstrated the successful formulation of Quercetin-loaded transdermal patches using HPMC, EC and PEG 400 by the solvent casting method. Among the formulations investigated, the optimized F6 Quercetin-loaded transdermal patch possesses satisfactory physicochemical characteristics, adequate drug incorporation, sustained drug release behaviour, acceptable morphological characteristics and short-term stability. The developed formulation may therefore serve as a promising approach for the controlled and sustained transdermal delivery of Quercetin. However, further studies such as extended stability studies, *ex vivo* permeation studies, skin irritation studies and *in vivo* investigations would be required to establish its complete transdermal performance and therapeutic potential.

ACKNOWLEDGEMENT

The authors are thankful to the correspondent, Sankaralingam Bhuvaneswari College of Pharmacy, Anaikuttam, Sivakasi, for providing excellent facilities to carry out the work.

REFERENCES

1. Mark R. Prausnitz, Robert Langer. Transdermal drug delivery. Nature Biotechnology. 2008;26(11):1261–1268.
2. Dipen Patel, Sunita A. Chaudhary, Bhavesh Parmar, Nikunj Bhura. Transdermal drug delivery system: A review. The Pharma Innovation Journal. 2012;1(4):66–75.
3. Marc B. Brown, Gary P. Martin, Stuart A. Jones, Franklin K. Akomeah. Dermal and transdermal drug delivery systems: Current and future prospects. Drug Delivery. 2006;13(3):175–187.
4. Patel K, Patel J, Zaveri M. Development, Optimization and Evaluation of Herbal Patch Formulation for Acne Treatment. International Journal of Pharmaceutical Investigation. 2022;13(1):74–81.
5. Michael E. Aulton and Kevin M. G. Taylor, editors. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 6th ed. London: Elsevier; 2022. pp.527.
6. Patrick J. Sinko, editor. Martin's Physical Pharmacy and Pharmaceutical Sciences. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2011. pp.492
7. British Pharmacopoeia Commission. British Pharmacopoeia 2012. 7th ed. Vol. V. London: The Stationery Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA); 2011. Appendix V A: Determination of Melting Point. pp. A282–A309.
8. Robert M. Silverstein, Francis X. Webster, David J. Kiemle, and David L. Bryce. Spectrometric identification of organic compounds. 8th ed. Hoboken, New Jersey: John Wiley & Sons; 2014:20-34.
9. Parhi R, Swain S. Transdermal evaporation drug delivery system: Concept to commercial products. Advanced Pharmaceutical Bulletin. 2018;8(4):535–550.
10. Howard C. Ansel, Loyd V. Allen Jr., and Nicholas G. Popovich. Pharmaceutical dosage forms and drug delivery systems. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2011.pp.187-235.
11. Gilbert S. Banker and Christopher T. Rhodes, editors. Modern Pharmaceutics. 4th ed. New York: Marcel Dekker; 2002.pp.275-283.
12. United States Pharmacopeial Convention. United States Pharmacopeia and National Formulary. Rockville, Maryland: United States Pharmacopeial Convention; 2020.pp.792.
13. Nicholas A. Peppas and Anil R. Khare. Preparation, structure and diffusional behavior of hydrogels in controlled release. Advanced Drug Delivery Reviews. 1993;11(1–2):1–35.
14. Loyd V. Allen Jr. The art, science and technology of pharmaceutical compounding. 5th ed. Washington, DC: American Pharmacists Association; 2016.pp.332.
15. A. H. Beckett and J. B. Stenlake. Practical Pharmaceutical Chemistry. 4th ed. London: Athlone Press; 1988.pp.19.
16. Jorg Siepmann and Florence Siepmann. Mathematical modelling of drug delivery. International Journal of Pharmaceutics. 2008;364(2):328–343.
17. Geoffrey D. Tovey. Pharmaceutical Formulation: The science and technology of dosage forms. Cambridge: Royal Society of Chemistry; 2018.pp.1-41
18. Shahiwala A, Misra A. Formulation design and *in vitro ex vivo* evaluation of transdermal patches of Cinnarizine. Drug Development and Industrial Pharmacy. 2018;44(1):105–115.
19. Joseph I. Goldstein, Dale E. Newbury, David C. Joy, Charles E. Lyman, Patrick Echlin, Eric Lifshin, Linda Sawyer, and Joseph R. Michael. Scanning electron microscopy and X-Ray microanalysis. 3rd ed. New York: Springer; 2003.pp.1-2
20. Saeedi M, et al. Formulation of Polymers-Based Methotrexate Patches and Investigation of the Effect of Various Penetration Enhancers: In Vitro, Ex Vivo and In Vivo Characterization. Polymers. 2022;14(11):2211.