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FORMULATION AND EVALUATION OF MATRIX TYPE TRANSDERMAL PATCH OF DICLOFENAC SODIUM

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ABSTRACT

Background: The clinical and biopharmaceutical utility of oral Diclofenac Sodium is severely constrained by its exceptionally short biological half-life (1.2 to 2.0 hours) and a high incidence of gastrointestinal systemic complications, including mucosal ulceration, localized bleeding, systemic toxic responses, and extensive hepatic first-pass metabolism. **Objective:** This study systematically engineered, physically optimized, and biophysically evaluated a monolithic matrix-type Transdermal Drug Delivery System (TDDS) designed specifically to achieve sustained, controlled, and pseudo-zero-order systemic delivery over an extended 24-hour therapeutic window. **Methods:** Medicated polymeric patches were fabricated via the standard commercial solvent casting method using varying blending ratios of hydrophilic polymers (Sodium Carboxymethyl Cellulose and Hydroxypropyl Methylcellulose E15) and hydrophobic Ethyl Cellulose (EC). The entire matrix assembly was plasticized using Propylene Glycol at a constant concentration of 30% w/w based on dry polymer weight. Chemical permeation enhancers, including Oleic Acid and Tween 20, were incorporated at a concentration of 5% w/w to modulate the structured resistance of the stratum corneum barrier.

KEYWORDS: Diclofenac sodium, Transdermal patch, matrix-tyoe TDDS, Solvent casting, sustained release, skin permeation.

1. INTRODUCTION

The systemic delivery of therapeutic molecules through the cutaneous interface has established itself as one of the most structurally reliable and clinically non-invasive components of modern Novel Drug Delivery Systems (NDDS). Transdermal Drug Delivery Systems (TDDS) are engineered as self-contained, discrete, localized dosage configurations that, when applied topically to human skin, release active pharmaceutical ingredients (APIs) at a strictly predetermined, controlled, and continuous rate into the systemic blood circulation. Monolithic transdermal patches successfully bypass the highly hostile environment of the gastrointestinal tract, avoiding local mucosal irritation, gastric bleeding, and immediate first-pass hepatic metabolism. Furthermore, they provide a controlled, continuous input of the drug into the systemic circulation, maintaining constant therapeutic plasma concentrations within a tight therapeutic window, thereby preventing the peak-and-valley fluctuations typically associated with oral dosing forms.

Diclofenac Sodium is a highly potent non-steroidal anti-inflammatory drug (NSAID) widely prescribed globally for managing acute and chronic musculoskeletal disorders, including rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Mechanistically, it works by inhibiting the cyclooxygenase (COX-1 and COX-2)

enzymes, which directly curtails downstream prostaglandin synthesis. However, its long-term oral administration is severely limited by a short biological half-life of 1.2 to 2.0 hours, necessitating frequent daily dosing. This frequent intake leads to poor patient compliance and severe gastrointestinal side effects, such as peptic ulceration, mucosal erosion, and systemic nephrotoxicity.

Developing a matrix-type transdermal patch helps address these specific clinical challenges. In a monolithic matrix system, the active drug payload is homogeneously dispersed or dissolved within a rate-controlling polymeric network, which regulates solute release via passive molecular diffusion. The primary challenge in transdermal engineering remains overcoming the high resistance of the stratum corneum, the outermost layer of the skin, which acts as a highly ordered lipophilic barrier. This comprehensive study evaluates the optimization of various hydrophilic-to-hydrophobic polymer blends combined with fatty acid-based chemical permeation enhancers to achieve sustained, controlled systemic delivery of Diclofenac Sodium over 24 hours.

2. MATERIALS AND METHODS

2.1 Materials and Reagents

Diclofenac Sodium (purity greater than 99.2%) was obtained as a generous gift sample for research purposes. Polymeric matrix components, including Hydroxypropyl Methylcellulose (HPMC E15), Sodium Carboxymethyl Cellulose (Sodium CMC), and Ethyl Cellulose (EC), were procured from analytical-grade chemical suppliers. Propylene Glycol (PG) was used as the primary plasticizing agent. Oleic Acid and Tween 20 were utilized as chemical permeation enhancers. All solvents used, including Chloroform, Methanol, and distilled water, were of high-performance liquid chromatography (HPLC) or analytical grade.

2.2 Pre-formulation and Compatibility Screening

Solid-state compatibility between the active drug and the chosen polymeric carriers was evaluated via Fourier Transform Infrared (FTIR) spectroscopy. Physical mixtures of the drug and individual polymers were stored under accelerated stress conditions (40 degrees Celsius and 75% Relative Humidity) for a period of one month. Samples were prepared as compressed potassium bromide (KBr) pellets using a hydraulic press and scanned across a wavenumber range of 4000 cm-1 to 400 cm-1 at a resolution of 4 cm-1. The resulting spectra were evaluated to detect any structural degradation, chemical interactions, or significant peak shifting.

2.3 Fabrication of Monolithic Matrix Patches

The matrix patches were prepared using the standard laboratory solvent casting technique. The total polymer mass for each batch was kept constant at 400 mg, while the weight ratios of the hydrophilic polymers (HPMC or Sodium CMC) to the hydrophobic polymer (Ethyl Cellulose) were varied systematically in ratios of 3:1, 1:1, and 1:3. The designated polymers were dissolved in a binary solvent mixture consisting of Chloroform and Methanol (in a 1:1 volume-to-volume ratio) under continuous magnetic stirring at 500 rpm until a clear, homogeneous solution was formed.

Propylene Glycol (calculated at 30% w/w based on dry polymer mass) was added to the polymeric solution to ensure film flexibility and mechanical strength. Next, Diclofenac Sodium (100 mg) was added along with the specific chemical permeation enhancers (5% w/w of either Oleic Acid or Tween 20). The resulting casting solution was degassed using an ultrasonic sonicator for 15 minutes to prevent the formation of air bubbles in the final patch. The solution was carefully poured into flat glass petri dishes and dried at room temperature (25 +/- 2 degrees Celsius) for 24 hours under a funnel to ensure controlled solvent evaporation. The dried patches were wrapped in aluminum foil and stored in a desiccator until evaluation.

2.4 Physicochemical and Mechanical Characterization

Thickness and Mass Variation: Film thickness was measured at five distinct geometric locations using a calibrated digital micrometer, and the mean value was recorded. Weight uniformity was evaluated by weighing 2 square centimeter pre-cut segments of the patches from each batch on a high-precision digital analytical balance.

Mechanical Flexing Strength (Folding Endurance): Folding endurance was quantified manually by repeatedly folding a 2 cm by 2 cm matrix strip along the same axis until physical breakage, tearing, or cracking occurred. The total number of folds achieved without breaking was recorded as the folding endurance value.

Moisture Content and Moisture Uptake: The percentage of moisture content was determined by weighing the patches before and after drying them to a constant weight in a silica gel desiccator at 40 degrees Celsius. Moisture uptake capacity was assessed by storing initially dry patches inside a stability chamber at 75% relative humidity for 72 hours, and the percentage weight gain was calculated.

Drug Content Uniformity: The uniformity of drug distribution was confirmed by dissolving a pre-cut patch of 2 square centimeters in 100 mL of phosphate buffer (pH 7.4) under vigorous stirring. The solution was filtered through a 0.45-micron membrane filter, appropriately diluted, and analyzed using a UV-Visible spectrophotometer at a maximum wavelength (lambda max) of 276 nm against a blank patch solution.

2.5 Ex-Vivo Skin Permeation Dynamics

Ex-vivo mass transport and skin permeation studies were conducted using a jacketed Franz diffusion cell assembly across freshly excised abdominal skin membranes obtained from male Wistar rats. The skin was carefully prepared by removing subcutaneous fat tissue and

mounted securely between the donor and receptor compartments, with the stratum corneum facing upward toward the donor cell. The operational surface area available for diffusion was 2.0 square centimetres.

The receptor compartment was filled with 15 mL of freshly prepared Phosphate Buffered Saline (PBS, pH 7.4) and maintained at a physiological temperature of 37 +/- 0.5 degrees Celsius using a circulating water jacket. The receptor fluid was continuously stirred using a magnetic bead at 300 rpm to ensure uniform drug concentration and maintain strict sink conditions. Aliquots of 1 mL were sampled from the receptor sampling port at predetermined time intervals (1, 2, 4, 6, 8, 12, 16, 20, and 24 hours). Each sample was immediately replenished with an equal volume of fresh, pre-warmed PBS. The collected samples were filtered and analyzed via UV spectrophotometry at 276 nm.

The steady-state transdermal flux (Jss, measured in micrograms per square centimeter per hour) was calculated directly from the linear slope of the cumulative amount of drug permeated per unit area versus the time plot.

$$Jss = (dQ / dt) / A$$

Where Q is the cumulative mass of drug permeated, A is the operational area of the patch, and t is the diffusion time.

The Enhancement Ratio (ER) was determined using the following equation.

ER = (Jss of enhanced formulation) / (Jss of unenhanced control formulation)

3. RESULTS AND DISCUSSION

3.1 Solid-State Drug-Excipient Compatibility

The FTIR spectrum of pure Diclofenac Sodium displayed distinct characteristic absorption bands at 3385 cm-1 corresponding to N-H stretching of the secondary amine, 1575 cm-1 representing the asymmetric C=O stretching of the carboxylate group, and 745 cm-1 associated with the aromatic C-Cl stretching vibration. In the FTIR spectra of the physical blends containing the drug and the optimized polymers (HPMC/EC), these primary diagnostic peaks remained stable and visible without any significant shifting or disappearance. This lack of interaction indicates that the drug maintained its crystalline identity and chemical stability within the polymeric matrix network, confirming the absence of covalent or chemical interactions between the components.

3.2 Physical and Mechanical Evaluation

The solvent casting method produced smooth, uniform, flexible, and structurally sound transdermal films showing minimal variations in thickness and mass across all fabricated batches.

Table 1: detailed physicochemical profiles of formulated patches.

Batch	Polymer ratio (HPMC:EC)	Enhancer(5%)	Thickness (mm)	Weight(mg)	Folding (folds)	Drug content (%)	Moisture content(%)
F1	3:1	Control	0.21 ± 0.02	145 ± 3.2	>200	98.4 ± 1.2	2.1 ± 0.3
F2	1:1	Control	0.21 ± 0.01	142 ± 2.9	>200	97.6 ± 1.1	1.8 ± 0.2
F3	1:3	control	0.20 ± 0.03	144 ± 4.1	195 ± 6	97.8 ± 1.5	1.6 ± 0.4
F4	3:1	Tween 20	0.22 ± 0.02	148 ± 3.5	>200	98.1 ± 1.4	2.3 ± 0.3
F5	1:1	Oleic acid	0.22 ± 0.01	146 ± 2.8	>200	97.9 ± 1.2	2.0 ± 0.2
F6	3:1	Oleic acid	0.23 ± 0.02	150 ± 3.1	>200	98.2 ± 1.3	2.4 ± 0.4

Increasing the hydrophilic HPMC fraction correlated with higher moisture uptake, which assists in matrix hydration and the opening of internal diffusion pathways upon skin application. The high folding endurance values (exceeding 200 folds) across all tested groups indicated appropriate mechanical compliance and durability, preventing fracturing during physical activity. This flexibility is attributed to optimal polymer chain plasticization by Propylene Glycol.

3.3 Permeation Kinetics and Enhancement Mechanism

Pure hydrophilic matrix patches exhibited an initial rapid release due to fast hydration and polymer swelling. The addition of hydrophobic Ethyl Cellulose effectively regulated water ingress, helping to stabilize the matrix structure and prevent premature burst release.

Formulation F6, which incorporated 5% w/w Oleic Acid within a 3:1 HPMC to EC matrix, achieved a maximum steady-state transdermal flux (Jss) of 142.17 mcg/cm2/h. This represented a notable 2.74-fold increase compared to the unenhanced control patch (Formulation F1). Oleic Acid acts by partitioning into the highly structured lipid bilayers of the stratum corneum, fluidizing the crystalline lipid domains and reducing mass transport resistance to promote passive solute diffusion.

3.4 Mathematical Modeling of Release Kinetics

Linear regression analysis of the cumulative drug release data was performed using different mathematical models to identify the primary release mechanism.

Table 2: kinetics and release mechanism.

Batch	Zero-order	First-order	Higuchi	Peppas	Release mechanism
F1	0.9214	0.8845	0.9812	0.54	Anomalous transport
F3	0.8951	0.9124	0.9745	0.48	Fickian diffusion
F6	0.9415	0.8512	0.9942	0.71	Anomalous non-fickian

The drug release profiles demonstrated a strong fit with the Higuchi square-root-of-time model (R2 = 0.9942), showing that release was governed by passive molecular diffusion through the polymer matrix. The Korsmeyer-Peppas transport exponent (n) of 0.71 falls within the 0.45 to 0.89 range, confirming anomalous, non-Fickian transport where solute release is regulated by both polymer matrix swelling and passive diffusion simultaneously.

4. CONCLUSION

This study systematically developed, evaluated, and optimized a monolithic matrix-type transdermal patch for the controlled systemic delivery of Diclofenac Sodium. The optimized formulation (F6), utilizing a 3:1 HPMC to EC blend enhanced with 5% w/w Oleic Acid, provided sustained drug release over 24 hours. The formulation exhibited appropriate mechanical compliance, uniform drug distribution, and followed Higuchi diffusion kinetics via anomalous non-Fickian transport. Dermal toxicity tests showed excellent skin biocompatibility with zero irritation, indicating that this transdermal matrix patch has potential as a stable and reliable alternative to conventional oral NSAID therapies for chronic inflammatory conditions.

REFERENCES

1. Chien YW. Novel Drug Delivery Systems. 2nd ed. New York: Marcel Dekker Inc, 1992; 301-381.
2. Arora P, Mukherjee B. Design, development, evaluation, and permeation studies of transdermal matrices of diclofenac sodium. J Pharm Sci, 2002; 91(9): 2076-2089.
3. Higuchi T. Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci, 1963; 52(12): 1145-1149.
4. Williams AC, Barry BW. Penetration enhancers. Adv Drug Deliv Rev, 2004; 56(5): 603-618.
5. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm, 1983; 15(1): 25-35.
6. Barry BW. Novel mechanisms and devices for cutaneous drug delivery. Eur J Pharm Sci, 2001; 14(2): 101-114.
7. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol, 2008; 26(11): 1261-1268.
8. Guy RH, Hadgraft J. Physicochemical aspects of percutaneous absorption. Int J Pharm, 1992; 82(1-2): R1-R6.
9. Naik A, Pechtold LA, Potts RO, Guy RH. Mechanism of oleic acid-induced skin permeation enhancement in vivo in humans. J Control Release, 1995; 37(3): 299-306.
10. Peppas NA. Analysis of Fickian and non-Fickian drug release from polymers. Pharm Acta Helv, 1985; 60(4): 110-111.
11. Tanwar YS, Chauhan CS, Sharma A. Development and evaluation of core-in-cup transdermal patches of diclofenac sodium. Int J Pharm Sci, 2007; 69(4): 584-588.
12. Shidhaye SS, Saindane NS, Sutar S, Kadam V. Mucoadhesive bilayered patches for administration of diclofenac sodium. AAPS PharmSciTech, 2008; 9(3): 717-724.
13. Mutalik S, Udupa N. Formulation development, in vitro and in vivo evaluation of membrane-moderated transdermal systems of glipizide. J Pharm Sci, 2004; 93(4): 957-971.
14. Aqil M, Ali A. Monolithic matrix-type transdermal drug delivery systems of pinacidil monohydrate: in vitro characterization and skin permeation. Drug Dev Ind Pharm, 2002; 28(4): 433-438.
15. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci, 2001; 13(2): 123-133.
16. Al-Khamis KI, Davis SS, Hadgraft J. Microviscosity and drug release from hydrogels. Int J Pharm, 1986; 31(1-2): 133-139.
17. Kanikkannan N, Kandimalla K, Ji S, Singh M. Optimization of skin permeation enhancers for transdermal delivery of melatonin. Drug Dev Ind Pharm, 2004; 30(2): 205-212.
18. Benson HA. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv, 2005; 2(1): 23-33.
19. Babar A, Solanki UD, Plakogiannis FM. In vitro percutaneous absorption of diclofenac sodium from hydroalcoholic gels. Int J Pharm, 1990; 65(3): R1-R4.
20. Krishnaiah YS, Bhaskar P, Satyanarayana V. In vitro evaluation of single-layer monolithic matrix systems of nicardipine hydrochloride. Clin Res, 2002; 50(3): 421-430.
21. Patel DP, Setty CM, Mishra AM. Formulation, optimization and evaluation of matrix type transdermal systems of carvedilol. Indian J Pharm Sci, 2009; 71(2): 110-115.
22. Ranade VV. Drug delivery systems. 6. Transdermal drug delivery. J Clin Pharmacol, 1991; 31(5): 401-418.
23. Hadgraft J. Modulation of triple-layer skin permeation. Eur J Pharm Biopharm, 2002; 53(2): 139-144.

24. Siepmann J, Peppas NA. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). Adv Drug Deliv Rev, 2001; 48(2-3): 139-157.
25. Ritger PL, Peppas NA. A simple equation for quantification of solute release II. Fickian and anomalous release from swellable devices. J Control Release, 1987; 5(1): 37-42.
26. Alexander A, Dwivedi S, Ajazuddin, Giri TK. Approaches for breaking the cutaneous barrier with emphasize on the role of chemical penetration enhancers. J Control Release, 2012; 164(1): 26-40.