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Formulation and Optimization of Magnoflorine-Loaded Transdermal Patches for Sustained Anti-Inflammatory Therapy

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Abstract:

Background: Inflammatory conditions such as rheumatoid arthritis and osteoarthritis are a major health concern worldwide. The existing oral and injectable formulations have limitations such as low bioavailability, systemic toxicity, and poor patient compliance, making the need for a continuous and non-invasive drug delivery system an area of prime importance.

Aim: The aim of the current study is to design and develop optimized transdermal patches of magnoflorine for controlled anti-inflammatory therapy.

Methods: Transdermal patches of magnoflorine were prepared using hydroxypropyl methylcellulose (HPMC) and ethyl cellulose (EC) using the solvent casting method. Polyethylene glycol 400 was used as a plasticizer and oleic acid as a permeation enhancer. The formulation was optimized by changing the ratio of the polymers, plasticizer, and enhancer. The patches were tested for their physical properties, thickness, weight, folding endurance, moisture content, drug content uniformity, in vitro drug release, and stability. The release kinetics of the drug was studied using zero-order, first-order, Higuchi, and Korsmeyer-peppas equations.

Results: The optimized formulation (F3) had a uniform thickness of 0.25 mm, excellent folding endurance of 260 cycles, and high drug content uniformity of 98.4%. In vitro release studies revealed the sustained release of drugs up to 96.2% in 24 hours, following diffusion-controlled Higuchi kinetics. Stability studies revealed negligible changes in appearance, drug content, and release characteristics for three months.

Conclusion: Magnoflorine transdermal patches provide a stable, non-invasive, and sustained-release platform for chronic anti-inflammatory therapy, enhancing efficacy and patient compliance while minimizing systemic side effects.

Keywords: Anti-inflammatory therapy; Drug delivery systems; HPMC–ethyl cellulose matrix; Magnoflorine; Sustained release; Transdermal patches.

Introduction:

Inflammation is a natural biological defence mechanism against tissue damage and infection; however, chronic inflammation is a major contributing factor in the development of several chronic disorders [1]. Chronic inflammatory diseases like rheumatoid arthritis, osteoarthritis, cardiovascular diseases, inflammatory bowel

disease, and neurodegenerative diseases are a major global health concern [2,3]. The World Health Organization states that chronic inflammatory diseases contribute to many non-communicable diseases, which are the cause of 74% of global deaths every year [4]. Rheumatoid arthritis affects 1% of the global population, and osteoarthritis affects over 500 million people worldwide, and the numbers are steadily rising due to an increase in the average age of the population and lifestyle changes [5]. In India, musculoskeletal and inflammatory diseases affect 22-25% of the adult population [6], which emphasizes the need for effective and patient-friendly long-term treatment modalities.

Conventional pharmacotherapy for inflammatory diseases involves mainly oral or parenteral routes of drug administration. Although oral drug delivery is quite popular, it has been associated with limitations such as poor bioavailability, gastrointestinal irritation, extensive first-pass metabolism, and fluctuating blood concentrations of the drug [7]. These limitations have often led to frequent dosing, thereby increasing the risk of side effects and lowering patient compliance, especially in long-term treatment. Parenteral drug delivery is invasive and not recommended for long-term use. Therefore, there is an urgent need for other drug delivery systems that can offer sustained drug effects with fewer systemic side effects.

Transdermal drug delivery systems (TDDS) have been found to be a promising non-invasive method for systemic drug delivery [8,9]. By delivering the drug across the skin and into the systemic circulation, transdermal patches overcome the degradation of drugs in the gastrointestinal tract and the first-pass effect of the liver. Transdermal drug delivery systems also have other advantages such as less frequent dosing, improved patient compliance, ease of administration, and easy discontinuation of drug therapy in case of an adverse reaction [10]. These advantages make transdermal patches an ideal choice for the treatment of chronic inflammatory conditions, where it is necessary to maintain a constant level of the drug in the plasma.

Magnoflorine is a naturally occurring quaternary aporphine alkaloid in several medicinal herbs like Tinospora cordifolia, Coptis chinensis, and Sinomenium acutum [11,12]. It has received considerable attention from the scientific community because of its diverse pharmacological properties, especially its anti-inflammatory, antioxidant, neuroprotective, antidiabetic, and immunomodulatory properties. The anti-inflammatory property of magnoflorine is mainly ascribed to its ability to suppress the production of pro-inflammatory mediators like nitric oxide, prostaglandins, and cytokines like TNF-α, IL-1β, and IL-6, along with the modulation of intracellular signaling pathways like NF-κB and MAPK [13,14]. However, the promising pharmacological properties of magnoflorine are yet to be exploited in the therapeutic field due to its low oral bioavailability, high metabolism rate, short biological half-life, and hydrophilic nature, which does not allow it to permeate through the cell membrane efficiently.

Transdermal delivery offers a promising approach to overcome these pharmacokinetic constraints by facilitating sustained and controlled drug release, along with minimizing systemic exposure and dosing intervals [15]. Nevertheless, the strong barrier property of the stratum corneum creates difficulties in the transdermal delivery of hydrophilic drugs such as magnoflorine. Thus, appropriate formulation development and optimization of polymers, plasticizers, and penetration

enhancers are required to improve drug permeation and provide optimal mechanical and release properties. In this context, the current study proposes the development and optimization of transdermal patches loaded with magnoflorine using a solvent casting method. The primary aim is to design and develop a stable and efficient transdermal delivery system that can sustain the delivery of magnoflorine for the treatment of chronic inflammatory diseases.

Materials and Methods

Materials

Magnoflorine was obtained from a reputed commercial supplier Sigma-Aldrich, USA Hydroxypropyl methylcellulose (HPMC K15M) and ethyl cellulose obtained from Loba Chemie Pvt. Ltd., Mumbai, India was used as film-forming polymers. Polyethylene glycol 400 (PEG 400) obtained from Merck Life Science Pvt. Ltd., India was employed as a plasticizer, and oleic acid obtained from Sigma-Aldrich, USA was used as a permeation enhancer. Ethanol and distilled water obtained from laboratory supply were used as solvents for formulation development. All chemicals and reagents were of analytical grade used.

Preformulation Studies

Organoleptic Evaluation: Magnoflorine was evaluated for its physical characteristics, including color, appearance, odor, and taste, by visual inspection to confirm its suitability for formulation.

Solubility Studies: The solubility of magnoflorine was determined in distilled water, ethanol, methanol, and phosphate buffer pH 7.4 using the shake-flask method. Excess drug was added to each solvent and shaken at 25 ± 2 °C for 24 h to assess solubility behavior.

Melting Point Determination: The melting point of magnoflorine was determined by the capillary method using a digital melting point apparatus to confirm drug purity.

Drug–Excipient Compatibility Studies: Compatibility between magnoflorine and formulation excipients was evaluated using Fourier Transform Infrared (FTIR) spectroscopy. FTIR spectra of pure drug, polymers, and their physical mixtures were recorded over a range of 4000–400 cm^{-1} to detect any possible chemical interactions.

UV Spectral Analysis: The UV absorption spectrum of magnoflorine was recorded between 200–400 nm using a UV-visible spectrophotometer to determine the wavelength of maximum absorbance (λmax). A calibration curve was prepared in phosphate buffer pH 7.4 over a concentration range of 5–50 µg/mL, and linearity was assessed for quantitative estimation.

Preparation of Magnoflorine-Loaded Transdermal Patches

Magnoflorine-loaded transdermal patches were prepared using the solvent casting method. HPMC K15M and ethyl cellulose were dissolved in a 7:3 ethanol–water mixture under continuous stirring to form a uniform polymeric solution. Magnoflorine was separately dissolved in the same solvent and incorporated into the polymer solution with constant stirring for homogeneous drug distribution. PEG 400 and oleic acid were added as a plasticizer and permeation enhancer, respectively. The resulting solution was degassed, cast onto a leveled glass surface, and allowed to dry at room temperature. Dried films were cut into uniform patches and stored in a desiccator until further evaluation.

Optimization of Formulation

Optimization of transdermal patches was carried out by varying polymer ratios, plasticizer concentration, and permeation enhancer content. The prepared formulations

were evaluated based on physicochemical properties, mechanical strength, drug content uniformity, and in vitro drug release behavior. The optimized formulation was selected based on sustained drug release and acceptable mechanical characteristics.

Characterization of Transdermal Patches

Physical Appearance: All patches were visually examined for color, transparency, surface smoothness, flexibility, and the presence of any visible defects such as cracks or air bubbles.

Thickness Uniformity: Patch thickness was measured at different points using a digital micrometer. The mean thickness and standard deviation were calculated to assess uniformity.

Weight Variation: Individual patches were weighed using an analytical balance. The average weight and standard deviation were calculated to evaluate uniform distribution of drug and excipients.

Folding Endurance: Folding endurance was determined by repeatedly folding the patch at the same point until it broke or showed visible cracks. The number of folds required to break the patch was recorded as an indicator of mechanical strength and flexibility.

Moisture Content: Moisture content was determined by weighing the patches before and after storage in a desiccator containing calcium chloride for 24 h. Percentage moisture content was calculated based on weight difference.

Drug Content Uniformity: A known area of the patch was accurately cut and dissolved in a suitable solvent. The solution was filtered and analyzed using UV-visible spectrophotometry at λmax. Drug content was expressed as a percentage of the theoretical value.

In Vitro Drug Release Studies

In vitro drug release studies were performed using a **Franz diffusion cell**. The transdermal patch was placed between the donor and receptor compartments with the drug-loaded side facing the receptor medium. Phosphate buffer pH 7.4 was used as the receptor medium and maintained at 37 ± 0.5 °C with continuous stirring. Samples were withdrawn at predetermined intervals and replaced with fresh medium to maintain sink conditions. The samples were analyzed spectrophotometrically to determine cumulative drug release.

Drug Release Kinetic Analysis

The release data obtained from in vitro studies were fitted to various kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models, to elucidate the drug release mechanism.

Stability Studies

Stability studies of the optimized transdermal patch formulation were conducted according to ICH guidelines. Patches were stored at 25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH for three months. At predetermined intervals, patches were evaluated for physical appearance, drug content, and in vitro drug release behavior.

Statistical Analysis

All experiments were performed in triplicate, and the results were expressed as mean ± standard deviation.

Results

The results of the present study focus on the formulation, characterization, and evaluation of magnoflorine-loaded transdermal patches developed using HPMC and ethyl cellulose. Preliminary assessments included the physical and chemical properties of the drug,

followed by systematic evaluation of patch attributes such as thickness, weight uniformity, mechanical strength, moisture content, and drug content. Additionally, in vitro drug release studies and kinetic modeling were performed to assess sustained release behavior, while stability studies were conducted to determine the robustness of the optimized formulation under standard and accelerated conditions.

Table 1 presents the organoleptic properties of magnoflorine, which are essential for preliminary assessment of drug quality and suitability for formulation. The drug appeared as a fine crystalline powder, indicating uniform particle morphology and good crystallinity, which are desirable for reproducible formulation processing. The pale-yellow color observed is consistent with the reported appearance of magnoflorine and suggests the absence of discoloration due to degradation or impurities. The absence of any characteristic odor indicates chemical stability and the lack of volatile contaminants. The slightly bitter taste is a typical characteristic of alkaloidal compounds and does not pose a concern for transdermal delivery since the dosage form bypasses the oral route. Overall, the organoleptic evaluation confirms that magnoflorine possesses acceptable physical attributes, purity, and stability, making it suitable for further pharmaceutical formulation and development into transdermal patches

Table 1: Organoleptic Properties of Magnoflorine

Property	Observation
Appearance	Fine crystalline powder
Color	Pale yellow
Odor	Odorless
Taste	Slightly bitter

Table 2 summarizes the solubility behavior of magnoflorine in various solvents. The drug was found to be freely soluble in distilled water and soluble in ethanol and methanol, indicating its hydrophilic nature and affinity toward polar solvents. Such solubility characteristics are advantageous for uniform drug dispersion in hydrophilic polymer matrices like HPMC. Moderate solubility in phosphate buffer pH 7.4 suggests adequate solubility under physiological conditions, which is critical for maintaining a concentration gradient necessary for transdermal diffusion. Adequate solubility at skin pH enhances drug release from the patch and subsequent permeation through the stratum corneum. The observed solubility profile therefore supports the feasibility of incorporating magnoflorine into transdermal delivery systems and indicates its potential for sustained and controlled drug release across the skin

Table 2. Solubility Profile of Magnoflorine in Different Solvents

Solvent	Solubility
Distilled water	Freely soluble
Ethanol	Soluble
Methanol	Soluble
Phosphate buffer (pH 7.4)	Moderately soluble

Table 3 compares the experimentally determined melting point of magnoflorine with reported literature values. The observed melting point range of 210–214 °C closely aligns with the reported range of 212–215 °C, indicating high purity and consistency of the drug sample used in the study. A narrow melting point range reflects uniform crystalline structure and absence of significant impurities or degradation products. Any substantial deviation in melting point could indicate contamination or polymorphic changes; however, the close agreement confirms the authenticity and quality of magnoflorine. This result validates the suitability of the drug for formulation studies and ensures reliability of subsequent experimental outcomes. Hence, the melting point analysis serves as a critical quality control parameter supporting the integrity and stability of the drug substance employed for transdermal patch development.

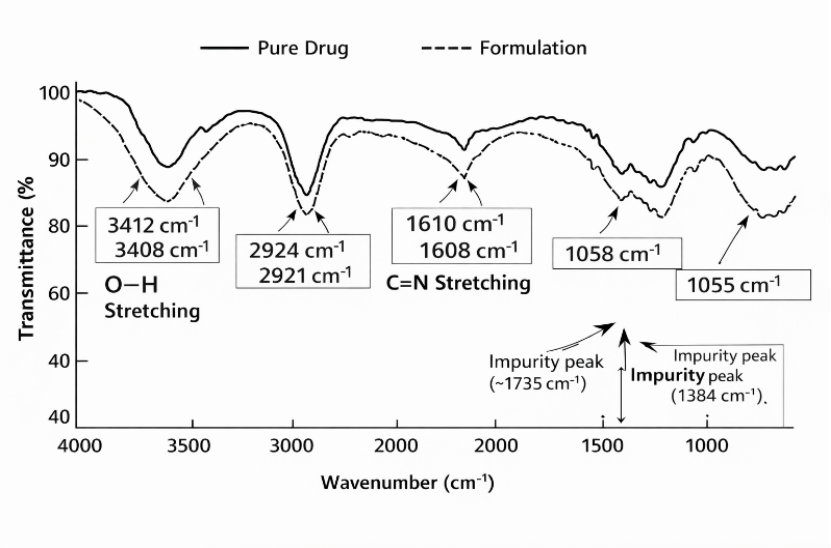
Table 3. Melting Point of Magnoflorine

Parameter	Observed Value (°C)	Reported Value (°C)
Melting point	210–214	212–215

Table 4 represents the FTIR compatibility study of magnoflorine with formulation excipients. The characteristic absorption peaks corresponding to functional groups such as O–H, C–H, C=N, and C–O were retained in both the pure drug and the formulation spectra, with only minor shifts in wavenumbers. These slight variations are typically attributed to physical interactions such as hydrogen bonding rather than chemical incompatibility. Importantly, no disappearance or formation of new peaks was observed, indicating the absence of chemical interactions or degradation during formulation. Preservation of the drug's functional groups confirms chemical stability and compatibility with selected polymers and excipients. These findings demonstrate that magnoflorine remains structurally intact within the transdermal patch matrix, thereby supporting the formulation's stability and suitability for sustained drug delivery applications.

Table 4. FTIR Compatibility Study of Magnoflorine

Functional Group	Pure Drug (cm^{-1})	Formulation (cm^{-1})
C–O stretching	1058	1055
C=N stretching	1610	1608
O–H stretching	3412	3408
C–H stretching	2924	2921



Graph 1. FTIR Compatibility Study of Magnoflorine

Table 5 illustrates the UV spectral characteristics of magnoflorine. The drug exhibited a sharp and well-defined absorption peak at 272 nm within the scanned wavelength range of 200–400 nm, confirming the presence of characteristic chromophoric groups. The sharpness of the peak and absence of additional peaks indicate high purity and minimal interference from impurities or degradation products. The absorbance value of 1.014 at a concentration of 50 µg/mL reflects strong UV absorption, making the drug suitable for spectrophotometric analysis. Identification of a distinct λmax is crucial for developing an accurate and reliable analytical method. These findings confirm that UV-visible spectrophotometry is an appropriate technique for quantitative estimation of magnoflorine in drug content analysis and in vitro drug release studies.

Table 5. UV Spectral Characteristics of Magnoflorine

Parameter	Observation
Wavelength range (nm)	200–400
λmax (nm)	272
Absorbance (50 µg/mL)	1.014
Purity indication	Sharp peak, no impurities

Table 6 outlines the composition of magnoflorine-loaded transdermal patches formulated with varying concentrations of polymers, plasticizer, and permeation enhancer while maintaining a constant drug load. Systematic variation in HPMC and ethyl cellulose concentrations allowed evaluation of their influence on mechanical strength, drug release, and overall patch performance. Incremental changes in PEG 400 and oleic acid concentrations were designed to optimize flexibility and enhance transdermal permeation. This formulation strategy enables clear comparison of physicochemical and release characteristics among formulations. Maintaining a constant drug dose ensures that observed differences in performance can be attributed solely to changes in excipient composition. Thus, the formulation design provides a rational basis for optimization and selection of the most effective transdermal patch.

Table 6. Composition of Magnoflorine-Loaded Transdermal Patches

Formulation	Drug (mg)	HPMC (mg)	EC (mg)	PEG 400 (% w/w)	Oleic Acid (% w/w)
F1	50	300	100	20	2
F2	50	350	150	25	3
F3	50	400	200	30	4
F4	50	450	250	25	5
F5	50	500	300	20	3

Table 7 summarizes the physical appearance of magnoflorine transdermal patches. Variations in color, surface texture, and flexibility were observed across formulations due to differences in polymer concentration. Formulations F1 and F2 exhibited transparent, smooth, and flexible films, indicating efficient polymer blending and adequate plasticization. Formulation F3 showed slightly opaque but uniform films with excellent flexibility, suggesting an optimal balance between polymer content and plasticizer concentration. In contrast, formulations F4 and F5 appeared opaque with reduced flexibility and rough surface texture, likely due to higher polymer load leading to a denser matrix. Overall, all patches were intact and free from visible defects, confirming the effectiveness of the solvent casting technique in producing uniform transdermal films.

Table 7. Physical Appearance of Magnoflorine Transdermal Patches			
Formulation	**Color**	**Surface Texture**	**Flexibility**
F1	Transparent	Smooth	Good
F2	Transparent	Smooth	Very good
F3	Slightly opaque	Uniform	Excellent
F4	Opaque	Uniform	Good
F5	Opaque	Rough	Moderate

Table 8 presents the thickness uniformity of the prepared transdermal patches. A gradual increase in thickness from F1 to F5 was observed, which directly correlates with increasing polymer concentration. Low standard deviation values across all formulations indicate consistent film casting and uniform distribution of polymers. Uniform thickness is a critical parameter as it directly influences drug content uniformity and release kinetics. Excessive variation in thickness could result in inconsistent dosing and unpredictable drug release; however, the observed results demonstrate excellent control over formulation variables. These findings confirm the reliability and reproducibility of the solvent casting method and indicate that the prepared patches possess suitable dimensional uniformity for transdermal drug delivery.

Table 8. Thickness Uniformity of Transdermal Patches	
Formulation	**Thickness (mm) ± SD**
F1	0.21 ± 0.02
F2	0.23 ± 0.01
F3	0.25 ± 0.02
F4	0.27 ± 0.03
F5	0.30 ± 0.02

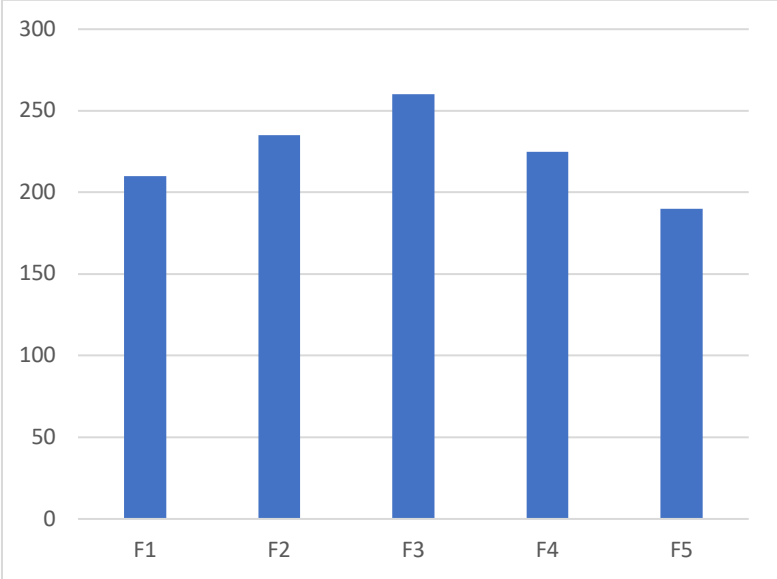
Table 9 illustrates the weight variation among different transdermal patch formulations. A progressive increase in average patch weight from F1 to F5 was observed due to higher polymer content. The low standard deviation values indicate uniform distribution of drug and excipients throughout the patch matrix and consistent solvent evaporation during film formation. Weight uniformity is essential to ensure dose accuracy and reproducibility of therapeutic effects. The observed results demonstrate that the formulation method employed provides good control over patch composition and mass. All formulations complied with acceptable limits for weight variation, indicating that the prepared patches are suitable for further evaluation and potential scale-up.

Table 9. Weight Variation of Transdermal Patches	
Formulation	**Weight (mg) ± SD**
F1	310 ± 4.2
F2	325 ± 3.8
F3	340 ± 5.1
F4	360 ± 4.7
F5	385 ± 5.4

Table 10 represents the folding endurance values of magnoflorine transdermal patches, reflecting their mechanical strength and flexibility. Folding endurance values ranged from 190 to 260, indicating that all formulations possessed sufficient flexibility to withstand repeated handling without cracking or breaking. Formulation F3 exhibited the highest folding endurance, suggesting optimal polymer–plasticizer interaction and superior mechanical integrity. Lower folding endurance observed in F5 may be attributed to increased rigidity due to

higher polymer concentration. Adequate folding endurance is crucial for ensuring patient compliance and durability during application. Overall, the results indicate that polymer concentration significantly influences the mechanical properties of transdermal patches.

Table 10. Folding Endurance of Transdermal Patches	
Formulation	**Folding Endurance**
F1	210
F2	235
F3	260
F4	225
F5	190



Graph 2. Folding Endurance of transdermal Patches

Table 11 shows the moisture content of magnoflorine transdermal patches. A gradual increase in moisture content from F1 to F5 was observed, likely due to higher concentrations of the hydrophilic polymer HPMC. Moisture content within acceptable limits is desirable as it helps maintain patch flexibility and prevents brittleness during storage. Excessive moisture could compromise stability, while insufficient moisture may cause cracking; however, all formulations demonstrated balanced hygroscopic properties. These results indicate good stability and suitability of the patches for storage under normal conditions. The controlled moisture content further supports the mechanical integrity and performance consistency of the transdermal patches.

Table 11. Moisture Content of Transdermal Patches	
Formulation	**Moisture Content (%) ± SD**
F1	3.2 ± 0.4
F2	3.8 ± 0.3
F3	4.5 ± 0.2
F4	4.9 ± 0.5
F5	5.4 ± 0.4

Table 12 presents the drug content uniformity of magnoflorine transdermal patches. All formulations exhibited drug content within the acceptable pharmacopeial range of 90–110%,

indicating uniform drug distribution within the polymeric matrix. Minimal standard deviation values reflect reproducibility and accuracy of the formulation process. Formulation F3 demonstrated the highest drug content uniformity, suggesting optimal viscosity and polymer concentration that facilitated even drug dispersion. Slight variations observed among formulations may be due to differences in polymer concentration affecting drug distribution during casting. Overall, these results confirm the reliability of the formulation technique and ensure consistent dosing across patches.

Table 12. Drug Content Uniformity of Transdermal Patches

Formulation	Drug Content (%) ± SD
F1	94.3 ± 1.6
F2	96.1 ± 1.2
F3	98.4 ± 0.8
F4	95.6 ± 1.4
F5	92.8 ± 1.9

Table 13 depicts the cumulative percentage drug release profiles of magnoflorine from different formulations over 24 hours. All formulations exhibited sustained drug release, with gradual increase over time. Formulation F3 showed the highest cumulative release (96.2%), indicating an optimal balance between hydrophilic and hydrophobic polymers. Formulations with higher polymer content (F4 and F5) exhibited slower drug release due to increased matrix density, which restricted drug diffusion. These results confirm the influence of polymer concentration on release kinetics and identify F3 as the optimized formulation. The sustained release profile suggests suitability of the developed patches for once-daily transdermal therapy.

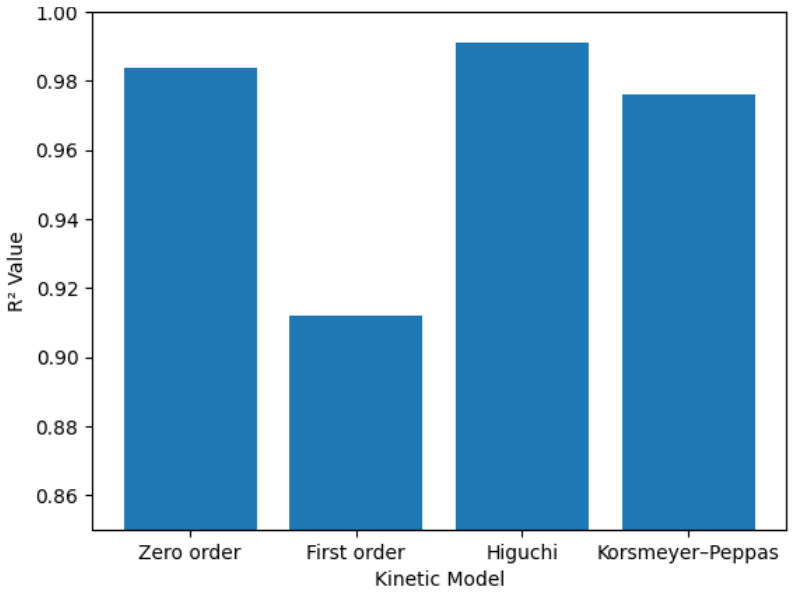
Table 13. Cumulative Percentage Drug Release of Magnoflorine

Time (h)	F1	F2	F3	F4	F5
1	12.4	15.3	18.6	14.2	10.8
4	32.5	38.6	45.9	36.4	28.7
8	54.2	61.8	70.4	58.6	49.2
12	68.3	75.6	84.7	72.3	61.5
24	82.4	88.9	96.2	85.1	73.6

Table 14 summarizes the drug release kinetic analysis of the optimized formulation F3. The highest correlation coefficient was observed for the Higuchi model (R^2 = 0.991), indicating diffusion-controlled drug release from the polymeric matrix. High R^2 values for the zero-order and Korsmeyer–Peppas models further support sustained and controlled release behavior. The relatively lower R^2 value for the first-order model suggests that drug release was not concentration-dependent. These findings indicate that magnoflorine release from the optimized transdermal patch is primarily governed by diffusion mechanisms, which are desirable for prolonged and predictable drug delivery.

Table 14. Drug Release Kinetic Models for Optimized Formulation (F3)

Model	R^2 Value
Zero order	0.984
First order	0.912
Higuchi	0.991
Korsmeyer–Peppas	0.976



Graph 3. Drug Release Kinetic Models for Optimized Formulation (F3)

Table 15 presents the stability study results of the optimized formulation F3 over three months. No visible changes in appearance were observed, indicating physical stability of the patches. A slight decrease in drug content was noted over time; however, values remained within acceptable limits, confirming chemical stability of magnoflorine within the patch matrix. Similarly, cumulative drug release at 24 hours showed minimal variation, indicating preservation of release characteristics during storage. These results confirm that the optimized formulation maintains its integrity, efficacy, and performance under specified storage conditions, supporting its suitability for long-term pharmaceutical application.

Table 15. Stability Study of Optimized Formulation (F3)

Parameter	Initial	1 Month	3 Months
Appearance	No change	No change	No change
Drug content (%)	98.4	97.9	97.2
Drug release (%) (24 h)	96.2	95.6	94.8

Discussion

The current study has successfully developed and optimized transdermal patches loaded with magnoflorine using hydroxypropyl methylcellulose (HPMC) and ethyl cellulose (EC) for sustained anti-inflammatory drug delivery. The preformulation study has confirmed that magnoflorine has favorable organoleptic characteristics, appropriate aqueous solubility, and a melting point very close to the literature values, which is an indication of its high purity and stability. This was also observed by Kumar et al., 2023, who stated that the physicochemical characteristics of the drug play a vital role in ensuring that the drug is evenly dispersed and has a predictable release in transdermal patches [16].

Solubility analysis showed that magnoflorine is freely soluble in water and partially soluble in phosphate buffer pH 7.4, which is beneficial for sustaining a concentration gradient in the skin. Patel 2017 observed similar solubility properties for hydrophilic alkaloidal compounds, indicating that such properties are helpful for efficient diffusion from polymeric matrices in transdermal systems [17] . The FTIR compatibility test showed the retention of characteristic functional groups of magnoflorine in the prepared transdermal patches, indicating the lack of chemical interaction with excipients. These results are in agreement with the observations of Wani et al., 2022, who found no significant drug-polymer interactions in EC-

HPMC-based transdermal systems, confirming the chemical stability of matrix systems [18] .

The solvent casting method used produced smooth, homogeneous, and flexible transdermal patches. The differences in polymer concentration greatly affected the physical properties of the patches, including thickness, weight, flexibility, and surface smoothness. Higher polymer concentrations resulted in thicker and more robust films but made them less flexible. Similar observations were made by Varma et al., 2004, who showed that higher polymer concentrations result in a higher density of the matrix, making it less elastic and slowing down drug diffusion [19]. The optimized formulation F3 had the optimal ratio of flexibility and mechanical properties.

Mechanical evaluation showed that all formulations had a satisfactory folding endurance, with the highest value being in F3. This result is in line with the results of Sharma and Singh, 2022, who found that the folding endurance of transdermal patches increased with the incorporation of optimal concentrations of plasticizer and hydrophilic polymers [20]. The moisture content of all formulations was found to increase with the increase in HPMC concentration, which is expected due to the hygroscopic properties of HPMC. Similar results were obtained by Desai et al., 2025, who stated that controlled moisture content is desirable to maintain the flexibility of the patches and avoid brittleness [21].

The drug content uniformity of all formulations was found to be within pharmacopeial limits, indicating that the drug is evenly distributed and the formulation process is reliable. Similar results were obtained by Borkhataria et al., 2024, who found that solvent casting results in uniform drug distribution when the viscosity of the polymer is optimized [22]. Among all the formulations, F3 had the highest drug content uniformity, which further confirms that it has the optimal composition.

In vitro drug release studies showed sustained release of magnoflorine over 24 hours for all formulations. Cumulative drug release was highest in formulation F3, which can be attributed to the hydrophilic-hydrophobic polymer blend combination, which favors diffusion. These results are consistent with the observations of Kulkarni et al., 2025, who found that the release of drugs was enhanced and sustained from matrix-type transdermal patches containing HPMC and EC blends [23].

Kinetic analysis of drug release showed that the optimized formulation followed the Higuchi model, indicating a diffusion-controlled release process, which is close to zero-order kinetics. Similar results have been obtained by Jain et al. 2005 for flurbiprofen and diclofenac transdermal systems, where the diffusion of drug through the polymeric matrix controlled the drug release [24].

Stability studies of the optimized formulation showed no significant difference in physical appearance, drug content, and release characteristics for a period of three months. The results are in line with the study of Bhowmik et al., 2012, which showed good stability of EC-HPMC transdermal patches under accelerated conditions [25]. Overall, the results of the current study are in close agreement with the previously reported transdermal drug delivery systems, thus establishing the fact that magnoflorine can be successfully formulated into a stable sustained release transdermal patch. The optimized formulation F3 showed desirable physicochemical characteristics, controlled drug release, and stability, thus establishing it as a promising candidate for sustained anti-inflammatory therapy.

Conclusion

The current research successfully formulated and optimized transdermal patches containing magnoflorine using HPMC and ethyl cellulose to deliver sustained anti-inflammatory effects. Preformulation analysis has revealed the purity, stability, and optimal solubility of the drug for its incorporation into polymeric matrices. The solvent casting technique has produced homogeneous, flexible, and defect-free patches, with mechanical strength, moisture, and drug content uniformity optimized in formulation F3. In vitro release analysis has shown sustained release of the drug for 24 hours, with release kinetics following the Higuchi model, suggesting diffusion-controlled release.

Stability analysis has further validated the physical and chemical stability of the optimized patches for a period of three months. Taken together, these results demonstrate the potential of magnoflorine transdermal patches as an effective, non-invasive, and patient-friendly drug delivery system for the long-term management of chronic inflammatory diseases, with enhanced therapeutic efficacy and compliance compared to existing oral or parenteral routes of drug administration.

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