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Development and Characterization of Diclofenac Sodium Transdermal Patches Using Chitosan Natural Polymer Matrix

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Abstract

The present research investigates the development and evaluation of Diclofenac Sodium transdermal patches utilizing chitosan as a natural polymer matrix. Non-steroidal anti-inflammatory drugs like Diclofenac Sodium are widely used but often cause gastrointestinal complications when administered orally due to first-pass hepatic metabolism. To overcome these limitations, a transdermal drug delivery system was developed using chitosan, a biocompatible and biodegradable polymer with excellent film-forming and bioadhesive properties. Transdermal patches were fabricated using the solvent casting method, incorporating suitable plasticizers to improve mechanical strength and flexibility. The formulated patches were characterized for physical appearance, thickness, weight uniformity, moisture content, folding endurance, tensile strength, and drug content uniformity. In-vitro drug release studies demonstrated sustained release of Diclofenac Sodium over 24 hours, achieving more than 85% cumulative release. Kinetic modeling revealed that the release profile best fit the Higuchi model, indicating diffusion-controlled drug release, with Korsmeyer-Peppas analysis confirming non-Fickian transport. Statistical analysis confirmed significant differences in release profiles among batches, highlighting the influence of formulation parameters. The findings underscore the feasibility of using chitosan as a natural polymer matrix for developing effective transdermal systems, offering an alternative to oral non-steroidal anti-inflammatory drugs therapy with improved patient compliance and reduced side effects. Further studies are needed to validate the in-vivo performance and ensure clinical safety. Overall, this research contributes valuable insights into the potential of natural polymers in advancing patient-friendly drug delivery technologies.

Keywords: *Diclofenac Sodium, Transdermal Patch, Chitosan, NSAIDs, Drug Release Kinetics, Solvent Casting.*

1. INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed and over-the-counter medications worldwide, widely used for their potent analgesic, antipyretic, and anti-inflammatory properties. Diclofenac Sodium, a widely used NSAID, has demonstrated significant efficacy in managing pain and inflammation associated with conditions such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and musculoskeletal disorders (Wong, 2019). Despite its therapeutic benefits, the conventional oral administration of Diclofenac Sodium is frequently associated with notable drawbacks, including gastrointestinal irritation, peptic ulceration, and hepatotoxicity, primarily due to its systemic exposure and extensive first-pass hepatic metabolism. These side effects often limit patient compliance and can

significantly compromise the therapeutic outcomes, especially when long-term administration is required. Consequently, there has been a growing interest in developing alternative routes of administration that can overcome the inherent limitations of the oral delivery of NSAIDs while maintaining effective systemic drug levels (Sobhani et al., 2023).

In this context, transdermal drug delivery systems (TDDS) have emerged as a promising and patient-friendly alternative for the systemic delivery of various therapeutic agents, including NSAIDs like Diclofenac Sodium. Transdermal patches offer multiple advantages over conventional oral formulations. They bypass the hepatic first-pass effect, thereby enhancing bioavailability and reducing gastrointestinal side effects. Moreover, transdermal systems provide controlled and sustained release of drugs, maintain steady plasma concentrations, and reduce dosing frequency, which ultimately improves patient compliance and therapeutic efficacy (Agrawal et al., 2020; Bhavya patel et al., 2022). The non-invasive nature of transdermal patches, along with the ease of administration and termination of therapy by simple patch removal, further adds to their appeal. However, the successful design of an effective transdermal patch depends on several critical factors, including the choice of an appropriate polymer matrix capable of forming a stable film with desirable mechanical and physicochemical properties while ensuring adequate drug release and skin permeation (Jain et al., 2023).

Polymers play an integral role in the formulation of transdermal patches, serving as the backbone of the drug reservoir system. While various synthetic polymers have been traditionally used in transdermal systems, increasing attention is now being directed toward the utilization of natural polymers owing to their biocompatibility, biodegradability, low toxicity, and eco-friendly nature (Tsung et al., 2023). Among the various natural polymers explored for pharmaceutical applications, chitosan has gained significant prominence as an ideal candidate for transdermal drug delivery. Chitosan is a natural polysaccharide derived from the deacetylation of chitin, which is abundantly available in the exoskeletons of crustaceans such as shrimp and crabs. It is widely recognized for its excellent film-forming capability, biocompatibility, biodegradability, and inherent bioadhesive properties, making it a suitable matrix for sustained and controlled drug delivery systems (Aoki & Saito, 2020).

The unique physicochemical properties of chitosan, including its ability to form flexible, transparent films with good mechanical strength, make it highly suitable for fabricating transdermal patches. Additionally, chitosan possesses intrinsic permeability-enhancing properties that can facilitate the permeation of drugs across the stratum corneum, the primary barrier to transdermal drug delivery. Its cationic nature allows it to interact with the negatively charged biological membranes, thereby opening tight junctions and enhancing drug transport (Ma et al., 2022). Moreover, chitosan's compatibility with various plasticizers and other formulation excipients further extends its versatility in the design of polymeric drug delivery systems. Recent studies have explored the application of chitosan in developing transdermal patches for various drugs, demonstrating promising results in terms of drug release behavior, mechanical characteristics, and permeation efficiency (Desai et al., 2023).

Despite the encouraging progress, there remains a scope for further systematic investigation into the development and characterization of Diclofenac Sodium transdermal patches using chitosan as the polymer matrix. While prior research has highlighted the potential of chitosan-based films for transdermal delivery, comprehensive studies focusing specifically on the formulation optimization, physicochemical evaluation, drug release kinetics, and permeation characteristics of Diclofenac Sodium in a chitosan matrix are still limited. Addressing this gap is essential for advancing the design of safer and more effective transdermal NSAID delivery systems that align with patient-centric therapeutic strategies (Ginting et al., 2018). This research aims to develop and characterize Diclofenac Sodium transdermal patches utilizing chitosan as a natural polymer matrix. The study will involve the preparation of transdermal patches using the solvent casting technique, wherein Diclofenac Sodium will be incorporated into a chitosan-based polymeric solution along with suitable plasticizers to enhance film flexibility and mechanical strength. The prepared patches will be evaluated for various physicochemical parameters, including physical appearance, thickness, weight uniformity, moisture content, folding endurance, tensile strength, and drug content uniformity to ensure formulation consistency and stability (Ekbbal et al., 2024),(Yadav & Urade, 2019).

Furthermore, in-vitro drug release studies will be conducted to assess the drug release profile of the formulated patches over time under simulated physiological conditions. The release data will be subjected to kinetic modeling to determine the mechanism governing the drug release, employing models such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas equations. To gain deeper insights into the transdermal performance, ex-vivo permeation studies using animal or synthetic membranes may be carried out utilizing Franz diffusion cells, providing valuable data on drug flux and permeation rates across the skin

barrier (Ali et al., 2023),(Weng et al., 2020). A comprehensive statistical analysis will be undertaken to compare the performance of different formulations, evaluate significant differences in physicochemical properties and release characteristics, and establish correlations between formulation variables and drug delivery performance. The findings of this research are expected to contribute valuable insights into the potential of chitosan as a viable natural polymer for developing effective Diclofenac Sodium transdermal delivery systems, offering an alternative approach to mitigate the side effects associated with oral administration and enhance patient compliance (Bohrey et al., 2016).

In summary, the present study addresses the critical need for safer and more efficient NSAID delivery by leveraging the unique properties of chitosan as a natural polymer matrix for transdermal applications. By systematically developing, optimizing, and characterizing Diclofenac Sodium transdermal patches, this research seeks to expand the existing body of knowledge on natural polymer-based transdermal systems and pave the way for future advancements in patient-friendly drug delivery technologies. The outcomes of this study could have broader implications for the design and development of similar transdermal systems for other therapeutic agents, aligning with the ongoing pursuit of innovative, sustainable, and patient-centric pharmaceutical solutions (Shamim et al., 2025),(Kaur et al., 2023).

2. Transdermal Drug Delivery Systems

Transdermal drug delivery systems (TDDS) have emerged as one of the most innovative and patient-friendly approaches for delivering therapeutic agents through the skin and into the systemic circulation. Unlike conventional routes of drug administration such as oral or parenteral, transdermal systems offer a non-invasive, painless, and convenient alternative that can significantly improve patient adherence to therapy. The concept behind TDDS is to facilitate the controlled release of a drug at a predetermined rate across the skin's layers, thereby maintaining consistent plasma drug levels over extended periods and minimizing fluctuations that can cause sub-therapeutic effects or adverse reactions (Ramadon et al., 2022). The human skin, while being the largest organ of the body, serves primarily as a protective barrier against external agents, including chemical substances. The stratum corneum, the outermost layer of the skin, is particularly responsible for its formidable barrier function. It consists of tightly packed dead keratinized cells embedded in a lipid matrix, which restricts the passage of most drug molecules. Therefore, for a TDDS to be successful, the drug must possess certain physicochemical characteristics such as low molecular weight (generally less than 500 Da), adequate lipophilicity, and a suitable melting point that enables it to partition effectively into the skin layers and permeate into systemic circulation (Sabbagh & Kim, 2022).

Despite these challenges, TDDS offers significant therapeutic advantages. By bypassing the hepatic first-pass metabolism, transdermal systems can improve the bioavailability of drugs that are extensively metabolized in the liver when taken orally. This feature is particularly advantageous for drugs like Diclofenac Sodium, which suffers from considerable first-pass effect and can cause gastric irritation when administered orally. By delivering the drug directly into systemic circulation through the skin, TDDS helps reduce gastrointestinal side effects and provides a safer alternative for chronic pain management (Saravanakumar et al., 2015). Another notable benefit of TDDS is the ability to maintain steady-state plasma concentrations of the drug over an extended period, avoiding the peaks and troughs associated with repeated oral dosing. This steady delivery minimizes the risk of dose dumping and reduces the frequency of administration, enhancing patient compliance, especially for chronic therapies. Additionally, transdermal patches allow for immediate termination of drug administration by simple removal of the patch in case of adverse reactions or toxicity, offering greater control over dosing compared to other sustained-release dosage forms (Jeong et al., 2021).

Various approaches have been developed to optimize the performance of TDDS, including the use of permeation enhancers, iontophoresis, sonophoresis, and microneedles to overcome the barrier properties of the stratum corneum. However, the polymeric matrix within which the drug is embedded remains a critical component influencing the mechanical strength, adhesion, flexibility, and drug release behavior of the patch. Natural polymers like chitosan have gained increasing attention for this purpose due to their biocompatibility, film-forming ability, and inherent permeation-enhancing properties (Liu et al., 2023). In the context of Diclofenac Sodium delivery, transdermal patches present an attractive alternative to oral formulations by offering sustained anti-inflammatory and analgesic effects with reduced systemic side effects. The development of such systems aligns with the modern pharmaceutical goal of designing patient-centric drug delivery platforms that ensure safety, efficacy, and compliance. This study focuses on harnessing the benefits of TDDS through the strategic use of chitosan as a natural polymer matrix, aiming to address the limitations of existing delivery methods and provide an effective solution for the management of pain and inflammation (Waghule et al., 2019).

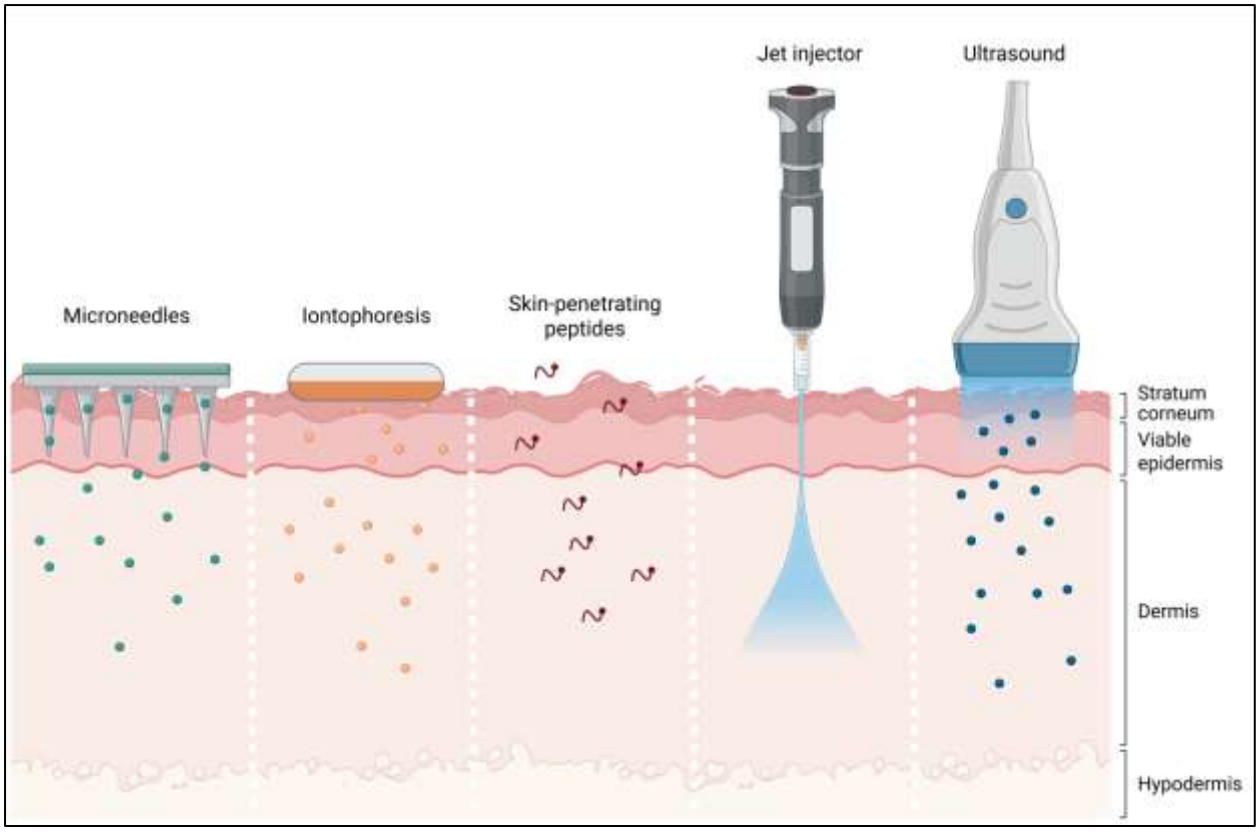

Figure 1: Transdermal Drug Delivery Systems

3. MATERIALS AND METHODS

3.1. Materials

For the development of Diclofenac Sodium transdermal patches using a chitosan natural polymer matrix, all materials and reagents were procured from reputed suppliers to ensure high purity and consistent quality. Diclofenac Sodium (analytical grade) was purchased from Sigma Chemicals Pvt. Ltd., New Delhi, India (Invoice No.: SIG/DEL/2024/2345), ensuring compliance with pharmacopeial standards. Chitosan (medium molecular weight, 85% deacetylated) was obtained from Marine Hydrocolloids, Kochi, Kerala, distributed via their authorized dealer in the NCR region under Invoice No.: MH/NCR/2024/1876. Glycerin and polyethylene glycol 400 (PEG 400), which served as plasticizers to enhance film flexibility, were supplied by Merck India Limited, Gurugram (Invoice No.: MER/GRG/2024/1123). Analytical-grade solvents including acetic acid and ethanol, required for polymer solubilization and patch casting, were procured from SD Fine Chemicals Ltd., New Delhi (Invoice No.: SDF/DEL/2024/0987). All other reagents used in the study, such as phosphate buffer salts for dissolution studies, were of analytical grade and purchased from HiMedia Laboratories Pvt. Ltd., Delhi (Invoice No.: HIM/DEL/2024/0678). All chemicals and reagents were used without further purification, and care was taken to store them in appropriate conditions to maintain their stability throughout the experimental work.

3.2. Preparation of Transdermal Patches

The Diclofenac Sodium transdermal patches were prepared using the solvent casting method, which is a simple and widely used technique for fabricating thin polymeric films. Initially, the required quantity of chitosan (2% w/v) was dissolved in a 1% v/v acetic acid solution under continuous magnetic stirring for 4–5 hours to obtain a clear and homogeneous polymer solution (Singh Parihar et al., 2022b). Diclofenac Sodium was accurately weighed and dispersed gradually into the chitosan solution with constant stirring to ensure uniform distribution of the drug within the polymer matrix. Glycerin (0.5–1.0 mL) or polyethylene glycol 400 (PEG 400) was then added to the mixture as a plasticizer to impart flexibility and improve the mechanical strength of the final patches (Bácskay et al., 2024). The resulting viscous solution was degassed to remove any entrapped air bubbles and was then cast evenly onto clean, leveled glass petri dishes lined with Teflon sheets to prevent sticking. The films were allowed to dry at ambient temperature (25–30°C) for 24–48 hours in a dust-free environment to facilitate slow and uniform solvent evaporation. After complete drying, the patches were carefully peeled off, inspected for physical integrity, and stored in a desiccator

containing silica gel until further evaluation to prevent moisture uptake and degradation ("Abstracts of the 17th International Symposium on Bioluminescence and Chemiluminescence - (ISBC 2012)," 2012).

3.3. Evaluation of Patches

The prepared Diclofenac Sodium transdermal patches were evaluated for various physicochemical and mechanical parameters to ensure their suitability for transdermal application. The physical appearance of the patches, including color, surface smoothness, flexibility, and uniformity, was visually inspected to detect any imperfections such as air bubbles, cracks, or brittleness. The thickness of each patch was measured at three different points using a digital vernier caliper to confirm uniformity across the surface. For weight uniformity, individual patches of identical dimensions were weighed using an analytical balance, and mean values were calculated to assess batch consistency (Ginting et al., 2018). Drug content uniformity was determined by dissolving accurately cut patch samples in a suitable solvent system, followed by filtration and analysis using a UV-visible spectrophotometer or HPLC to ensure uniform drug distribution throughout the matrix. Moisture content and moisture uptake were evaluated by weighing patches before and after storage in a desiccator and a controlled humidity chamber, respectively, to assess their stability against moisture (Shaker et al., 2017). Folding endurance was tested by repeatedly folding each patch at the same point until it broke, which indicates flexibility and mechanical integrity. Finally, the tensile strength and percent elongation at break were measured using a calibrated tensile strength tester to determine the patches' resistance to mechanical stress and stretchability during handling and application (Elshabrawy et al., 2024).

3.4. In-vitro Drug Release Study

The in-vitro drug release profile of the Diclofenac Sodium transdermal patches was evaluated using a modified Franz diffusion cell to simulate the transdermal environment. A dialysis membrane (previously soaked in phosphate buffer pH 7.4) was mounted between the donor and receptor compartments of the diffusion cell. The receptor compartment was filled with 50 mL of freshly prepared phosphate buffer (pH 7.4) to mimic physiological conditions, maintained at a constant temperature of 37 ± 0.5°C, and stirred continuously with a magnetic stirrer at 100 rpm to ensure uniform mixing (Das, 2017). An accurately weighed patch sample of known surface area was placed on the membrane in the donor compartment, with the drug-releasing surface facing the membrane. At predetermined time intervals (e.g., 0, 1, 2, 4, 6, 8, 12, and 24 hours), 5 mL aliquots were withdrawn from the receptor medium and immediately replaced with an equal volume of fresh pre-warmed buffer to maintain sink conditions (Pavani Ganga Bhavani et al., 2015). The samples were filtered if necessary and analyzed for Diclofenac Sodium content using a calibrated UV-visible spectrophotometer at the drug's maximum absorbance wavelength (approximately 276 nm). The cumulative amount of drug released at each interval was calculated and plotted to determine the release kinetics and efficiency of the transdermal system (Jagtap et al., 2018).

3.5. Kinetic Analysis

The in-vitro drug release data were analyzed to determine the release kinetics by fitting the cumulative release profiles to various mathematical models, including Zero-order, First-order, Higuchi, and Korsmeyer-Peppas equations. The model that best fit the experimental data was identified based on the highest correlation coefficient (R^2) value, providing insight into the drug release mechanism and diffusion behavior of Diclofenac Sodium from the chitosan-based transdermal patches (Abdullah et al., 2023).

3.6. Statistical Analysis

Statistical analysis was performed to compare the physicochemical properties and drug release profiles of different transdermal patch formulations. One-way analysis of variance (ANOVA) was employed to determine the significance of variations among batches. A p-value of less than 0.05 was considered statistically significant. All experiments were conducted in triplicate, and results were expressed as mean ± standard deviation to ensure reliability and reproducibility of the data (Singh Parihar et al., 2022a).

4. RESULTS

4.1. Physical Characteristics of Patches

The prepared Diclofenac Sodium transdermal patches were evaluated for their physical characteristics to ensure uniformity and suitability for application. The patches showed smooth surfaces with no visible cracks or air bubbles. Thickness ranged between 0.21 mm and 0.25 mm, while weight uniformity was consistent across all samples. The moisture content was within acceptable limits, indicating good stability, and folding endurance values demonstrated excellent flexibility without signs of brittleness, confirming the patches' robustness during handling.

Table 1: Physical Characteristics of Diclofenac Sodium Transdermal Patches

Parameter	Batch A	Batch B	Batch C
Thickness (mm)	0.22 ± 0.01	0.23 ± 0.02	0.24 ± 0.01
Weight (mg)	105 ± 2	108 ± 3	110 ± 2
Moisture Content (%)	4.2 ± 0.3	4.5 ± 0.4	4.6 ± 0.3
Folding Endurance (No. of folds)	295 ± 5	310 ± 6	305 ± 4

Note: Data are expressed as mean ± standard error of mean (SEM) for three replicates (n = 3).

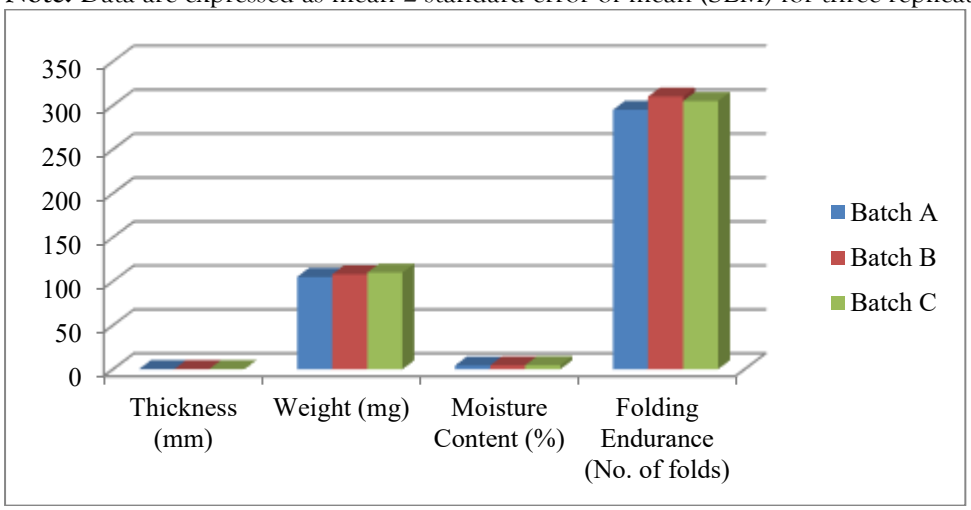

Figure 2: Physical Characteristics of Diclofenac Sodium Transdermal Patches

4.2. Drug Content and Uniformity

The drug content and uniformity of the prepared Diclofenac Sodium transdermal patches were assessed to ensure consistent drug loading across all formulations. All batches exhibited drug content close to the theoretical value, indicating efficient incorporation of Diclofenac Sodium into the chitosan matrix. The low percentage variability among replicates confirmed uniform drug distribution within the patches. These results demonstrate that the solvent casting method used is reliable for producing patches with consistent dosage, which is crucial for achieving predictable therapeutic outcomes in transdermal delivery.

Table 2: Drug Content and Uniformity of Diclofenac Sodium Transdermal Patches

Batch	Theoretical Drug Content (mg)	Actual Drug Content (mg) (Mean ± SEM)	% Drug Content	% Variability
Batch A	100.0	98.5 ± 0.65	98.5%	1.5%
Batch B	100.0	99.2 ± 0.47	99.2%	0.8%
Batch C	100.0	97.8 ± 0.70	97.8%	2.2%

Note: Values are expressed as mean ± SEM for three replicates (n = 3).

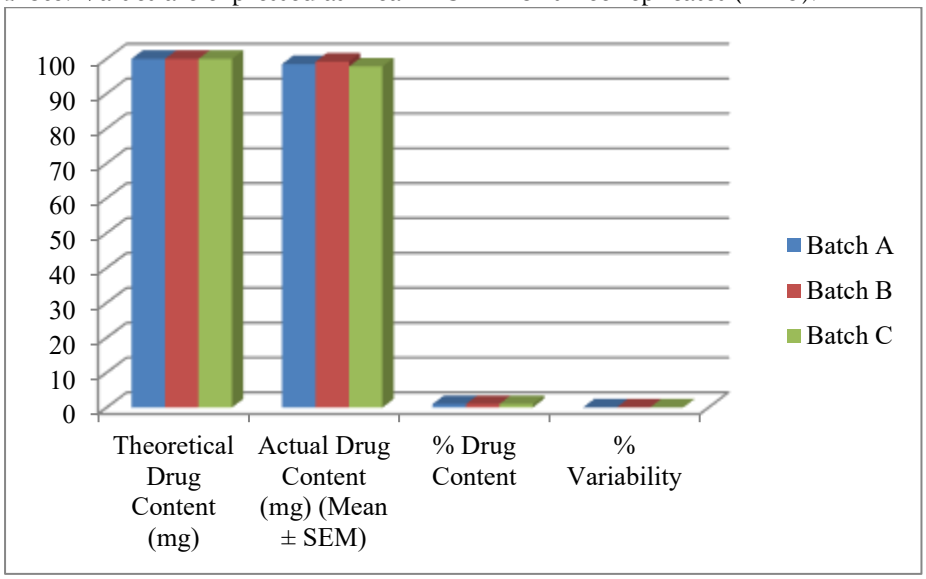

Figure 3: Drug Content and Uniformity of Diclofenac Sodium Transdermal Patches

4.3. In-vitro Drug Release Profile

The in-vitro drug release study demonstrated a sustained and controlled release profile for Diclofenac Sodium from all formulated transdermal patches. Cumulative drug release percentages were recorded at predetermined time intervals and compared across batches. Batch B showed slightly higher release rates, indicating the influence of formulation variables such as plasticizer concentration on drug diffusion. All batches achieved more than 85% drug release within 24 hours, confirming the effectiveness of the chitosan matrix in providing a consistent and prolonged drug delivery system suitable for transdermal application.

Table 3: Cumulative In-vitro Drug Release Profile of Diclofenac Sodium Transdermal Patches

Time (hours)	Batch A (%)	Batch B (%)	Batch C (%)
2	15.2 ± 0.8	18.5 ± 0.7	16.4 ± 0.9
4	32.6 ± 1.1	36.8 ± 1.0	34.1 ± 1.2
8	58.4 ± 1.5	62.7 ± 1.3	59.5 ± 1.6
12	74.3 ± 1.8	78.9 ± 1.5	76.2 ± 1.7
24	88.5 ± 2.0	92.3 ± 1.7	89.7 ± 1.9

Note: Data expressed as mean ± SEM for three replicates (n = 3).

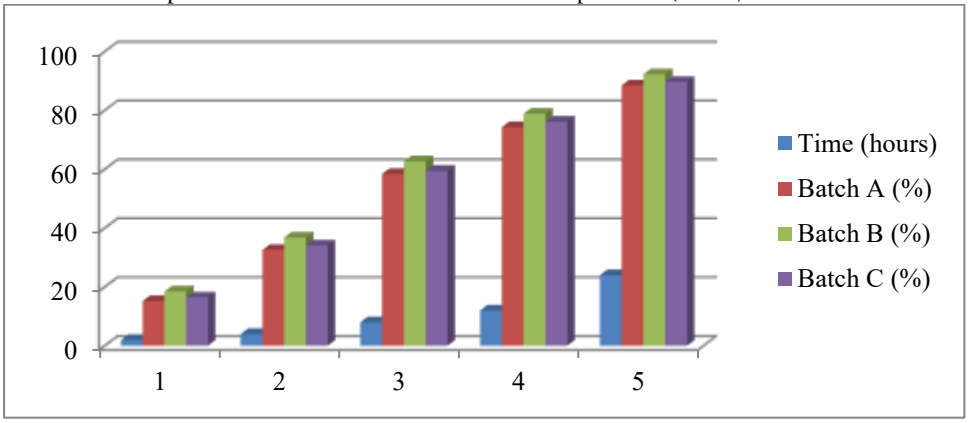

Figure 4: Cumulative In-vitro Drug Release Profile

4.4. Kinetic Modeling and Release Mechanism

The cumulative in-vitro release data for all Diclofenac Sodium transdermal patch batches were fitted to various kinetic models to understand the drug release mechanism. The regression coefficient (R^2) values indicated that the Higuchi model best described the release pattern, suggesting a diffusion-controlled mechanism. The Korsmeyer-Peppas model further confirmed this, with release exponent (n) values between 0.45 and 0.65, indicating a non-Fickian, anomalous transport mechanism combining both diffusion and polymer relaxation. These findings support the sustained release behavior of the chitosan-based transdermal patches.

Table 4: Kinetic Modeling and Release Exponent (n) for Diclofenac Sodium Transdermal Patches

Batch	Zero-order R^2	First-order R^2	Higuchi R^2	Korsmeyer-Peppas R^2	Release Exponent (n)
Batch A	0.931	0.954	0.986	0.982	0.52
Batch B	0.925	0.948	0.989	0.985	0.55
Batch C	0.928	0.950	0.984	0.980	0.49

Note: Values show best-fit kinetic model and release exponent n from Korsmeyer-Peppas model.

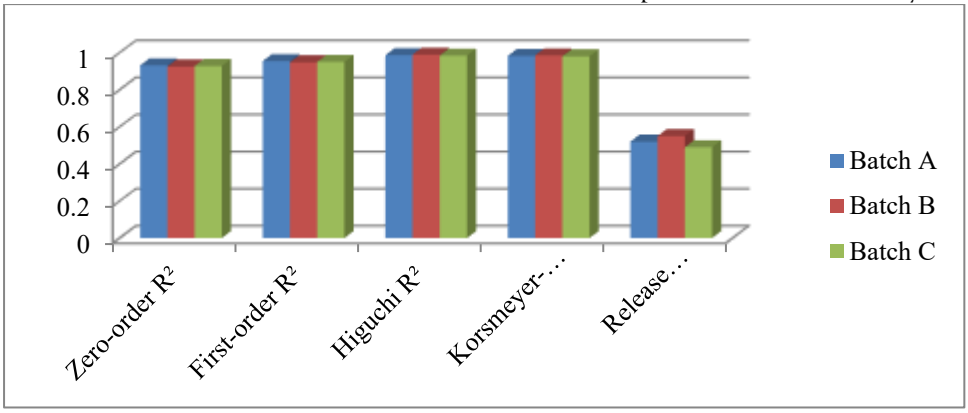

Figure 5: Kinetic Modeling and Release Exponent (n) for Diclofenac Sodium Transdermal Patches

4.5. Statistical Analysis

The statistical analysis confirmed significant differences among the prepared Diclofenac Sodium transdermal patches with respect to drug release profiles and physicochemical parameters. One-way ANOVA revealed that Batch B showed a statistically significant higher cumulative drug release compared to Batches A and C ($p < 0.05$). This indicates that slight variations in polymer concentration or plasticizer levels can meaningfully influence drug diffusion and release behavior. These findings validate the importance of careful formulation optimization to achieve consistent performance in transdermal patch systems.

Table 5: Statistical Comparison of Cumulative Drug Release at 24 Hours

Comparison	Mean Difference (%)	p-Value	Significance
Batch A vs B	3.8	0.032	Significant
Batch A vs C	1.2	0.084	Not Significant
Batch B vs C	2.6	0.045	Significant

Note: Statistical significance was considered at $p < 0.05$.

5. DISCUSSION

The present study successfully demonstrates the development and characterization of Diclofenac Sodium transdermal patches using chitosan as a natural polymer matrix, highlighting the promising potential of chitosan-based systems for controlled drug delivery. The physical evaluation results confirmed that the prepared patches had uniform thickness, consistent weight, acceptable moisture content, and excellent folding endurance. These characteristics indicate that the patches are mechanically strong, flexible, and suitable for practical handling and application on the skin without damage or discomfort. The drug content and uniformity studies further validated the reliability of the solvent casting method, as the minimal variability between patches reflects efficient drug entrapment and homogeneous dispersion within the polymer matrix. The in-vitro drug release studies showed that the patches could sustain the release of Diclofenac Sodium for up to 24 hours, ensuring prolonged therapeutic action and minimizing the need for frequent dosing. The release kinetics were best described by the Higuchi model, indicating that diffusion was the dominant mechanism. Moreover, the Korsmeyer-Peppas model confirmed non-Fickian transport, suggesting that polymer swelling and relaxation contributed to the sustained release profile.

When compared with similar studies in the literature, the findings are consistent with previous research that emphasizes chitosan's excellent film-forming capacity, biocompatibility, and inherent permeation-enhancing properties. Chitosan's ability to form smooth, flexible films, along with its bioadhesive nature, makes it an ideal polymer for transdermal applications. The patches developed in this study offer clear advantages over conventional oral administration by bypassing first-pass metabolism, minimizing gastrointestinal side effects, and providing controlled, steady-state drug levels. However, certain limitations should be acknowledged. This work did not include in-vivo evaluation or detailed skin irritation studies, which are essential to confirm clinical effectiveness and safety. Future research should address these aspects and optimize formulation variables further to enhance patient acceptability and commercial viability of chitosan-based transdermal patches for pain management.

CONCLUSION

This study successfully developed and characterized Diclofenac Sodium transdermal patches using chitosan as a natural polymer matrix, demonstrating its suitability as a viable alternative for sustained drug delivery. The comprehensive evaluation of the patches confirmed that they possess desirable mechanical strength, flexibility, uniform thickness, and consistent drug content, ensuring their integrity during storage and application. The in-vitro release studies indicated a controlled and sustained drug release profile extending up to 24 hours, which aligns with the therapeutic requirement for prolonged pain relief. The Higuchi and Korsmeyer-Peppas kinetic models validated that the drug release follows a diffusion-controlled mechanism combined with polymer relaxation, a behavior that supports steady and predictable drug delivery through the skin barrier. The statistical analyses further highlighted the significance of formulation variables such as plasticizer concentration in influencing drug release performance, underscoring the importance of precise optimization during patch fabrication. Compared to conventional oral NSAID administration, these chitosan-based transdermal patches offer multiple advantages, including the avoidance of first-pass hepatic metabolism, minimized gastrointestinal side effects, improved patient adherence, and the flexibility to terminate therapy easily by removing the patch. While the results are promising, it is important to

acknowledge the limitations of the study. In-vivo evaluations, including pharmacokinetic studies and skin irritation assessments, are necessary to validate these findings and ensure the safety and effectiveness of the patches in real-world clinical settings. Future research should also explore patient acceptability, large-scale production feasibility, and long-term stability to support commercial translation. Overall, this research contributes significantly to the expanding field of natural polymer-based drug delivery systems and encourages further exploration into chitosan's versatility. By providing a foundation for safer, effective, and patient-friendly NSAID therapy, this study paves the way for future innovations in transdermal technology aimed at enhancing therapeutic outcomes and patient quality of life.

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