ISSN: **3139-0854**

Effects of Various Polymer Ratios on the Preparation and Evaluation of Transdermal Patches of Anti-HIV Drugs

Soumyaranjan Sahoo[1]*, Sritam Behera[2]

[1] Assistant Professor, Department of Pharmaceutics, Nityananda College of Pharmacy, Sergarh, Baleshwar*
[2] Assistant Professor, Department of Pharmaceutics, Nityananda College of Pharmacy, Sergarh, Baleshwar
[1]* soumyaranjans710@gmail.com, Z beherasritam98@gmail.com

Abstract:

Transdermal drug delivery systems are attractive alternatives to standard oral antiretroviral therapy as they are characterized by prolonged drug release, enhanced patient compliance and preventance of first-pass metabolism. In the current paper, the researcher sought to examine how the different ratios of polymer influence the design and testing of transdermal patches with Tenofovir Alafenamide (TAF), a popular anti-HIV medication. The solvent cast method was used to prepare the patches with hydrophobic Eudragit RS100 and hydrophilic Hydroxypropyl Methylcellulose (HPMC) in various proportions. The patches formulated were assessed in terms of physicochemical properties, mechanical properties, uniform content of drugs and ability to release them in vitro, in vivo release and discharge, mechanological release rates, and stability. All the formulations had smooth and uniform films and acceptable weight variation, thickness, and surface pH. Mechanical analyses showed that the tensile strength was boosted with the addition of more Eudragit RS100 and flexibility and moisture uptake with more HPMC content. Ranging between 96-99, the drug content uniformity was consistent, and meant that there was homogeneous drug dispersion. The in vitro release experiments showed that the HPMC-rich patches had a fast rate of release and Eudragit-dominant patches had a slow rate of release. The mixed polymer formulation consisting of HPMC:Eudragit RS100 at a 50:50 ratio performed the best whereby the formulation sustained the release of TAF in more than 24 hours and controlled the release kinetics of TAF through diffusion. Ex vivo transdermal flux permeation analysis proved to be effective and lab stability analysis revealed no alteration in drug content and release profile within three months of accelerated conditions. These findings provide evidence that polymer ratio is a critical factor which determines the properties of patches and that optimized hydrophilic-hydrophobic polymer blend is capable of delivering Tenofovir Alafenamide on a sustained and constant basis. The transdermal system developed is a potential solution to alternatives in administering antiviral drugs and should be researched in more animal studies.

Keywords—Tenofovir Alafenamide; Transdermal patches; Polymer ratio; HPMC; Eudragit RS100; Solvent casting

ISSN: 3139-0854

1. INTRODUCTION

Transdermal drug delivery systems (TDDS) have become a new entrant that is likely to be a promising alternative to traditional orally and injectable routes particularly with chronic conditions that need prolonged levels of therapeutic levels and increased adherence by the patient. These delivery systems distribute the drugs throughout the body by avoiding first-pass hepatic hepatobiliary and limiting side effects commonly linked to oral intake of drugs (Karve et al., 2024). The overall construction of a transdermal patch is a polymeric structure regulating drug-release and permeation to the stratum corneum, which is the major obstacle to percutaneous absorption (Karve et al., 2024; Limenh et al., 2024).

With the HIV/AIDS case in consideration, viral control and better patient outcomes are only possible with the support of long-term antiretroviral therapy (ART). Nevertheless, there are frequent concerns related to poor compliance, varying plasma concentration, and adverse effects associated with daily oral regimens, which may undermine the efficacy of treatment as well as expose patients to risks of resistance (Puri et al., 2019). Anti-HIV drugs may benefit by the transdermal route with more reliable systemic concentrations, less complicated dosage, and the ability to release drugs over an extended period, thereby improving adherence and clinical control.

The polymers in TDDS are very important factors that determine patch performance. They are the support structure of the matrix or adhesive section and affect the important parameters like mechanical strength, flexibility, the ability to load drug molecules and release kinetics. Polymers may be either hydrophilic, hydrophobic or amphiphilic and each of the polymers gives the patch different physicochemical properties. Which proportion and mix of these polymers in a formulation may significantly influence the drug release rates and drug permeation profiles (Limenh et al., 2024; Karve et al., 2024). The activity of hydrophilic polymers is normally enhanced by the fact that it is capable of taking in moisture and swelling, thereby providing aqueous channels through which the drug can be diffused. Conversely, others can be hydrophobic polymers that however slows down release but offers better structural integrity (Limenh et al., 2024).

To achieve a compromise between controlled release and sufficient permeation and mechanical performance, it is hence necessary to optimize the ratios of polymers. Reports on alternative therapeutic systems have shown that different polymer formula ratios change significantly in vitro drug release profile, fold strength, and adhesive properties of transdermal systems (Limenh et al., 2024). This is of practical use in the case of anti-HIV medications, which in most cases require a very specific pharmacological level of plasma concentration to allow the drug to exert the anti-viral effect but with a little toxicity.

Although these theoretical benefits and the supporting evidence of the formulation science show these differences, a specific study of the effects of polymer ratios in the anti-HIV transdermal delivery is very limited. Most studies of transdermal have been based on model drugs or non-HIV therapeutics, and rather limited studies have translated this to antiretroviral drugs (Karve et al., 2024). The discussion of this gap is necessary to come up with viable TDDS platforms based on the specific pharmacokinetic requirements of anti-HIV agents.

We examine the effect of different ratios of the polymers in the preparation and testing of transdermal patches containing an anti-HIV medication in this research. This study will use systematic analysis of physicochemical characteristics, the release rates of drugs and their ability to permeate through skins to determine the best polymer compositions which will enhance their therapeutic effects and the general acceptability of these systems of delivering anti-HIV drugs via the transdermal route.

2. LITERATURE REVIEW

2.1 Principles of transdermal drug delivery and the primary role of polymers

Recent TDDS reports are still unanimous in recognising the polymer matrix as the actual determinant of patch integrity, drug as well as controlled release behaviour. Vaseem et al. (2023) stressed that polymers in TDDS should be biocompatible, drug-compatible, and capable of ensuring a constant distribution of the drug and being capable of delivering consistent mechanical performance during shelf life. Continuing on this base, Karve et al. (2024) emphasized the factor of polymer choice as it determines the diffusion of the drug, as well as the viability of patches to deliver long-acting agents, concluding that decisions in a formulation should consider drug solubility in the matrix, stability, adhesive properties, and the behavior of the skin interface. More current, Crasta et al. (2025) conducted a survey of the current approaches to TFDS, and they aligned with expectations under regulations, which has left no doubt that polymer systems should exhibit the identical quality properties (uniformity of content, adhesion, mechanical strength, and reproducible release) (Crasta et al., 2025). All this poetry is an argument in favor of polymer ratio optimization as a fundamental approach to formulation, as opposed to a trivial change in processing.

2.2 Polymer ratio as a formulation "lever" of patch physicomechanical properties

Several studies involving formulation (not limited to non-HIV drugs but applicable in principle) demonstrated that patches of different polymer ratios alter their thickness, weight change, folding strength, tensile strength, moisture absorption and the homogeneity of the film, which also change stability of release. As an illustrative case, Rajasekhar (2024) made patches of matrix in varying proportions of HPMC, Eudragit RL, and ethyl cellulose and reported that the template used is polymer blending to tune the film forming properties and release (Rajasekhar, 2024). Likewise, concerning the secondary polymers (including PVP or Eudragit grades), the article that provides applied formulation data on using HPMC to form films explains the influence of adjusting polymer concentration/ratio on analyzing the results of film formation and film properties such as flexibility and integrity (I.J.F.M.R., 2024). All these studies contribute to a unified conclusion: hydrophilic polymers have a higher propensity towards swelling and diffusion pathways, whereas hydrophobic polymers are a more effective strengthening material, and diffusion is slowed down by them--thus the relationship between these two parameters is the feasible adjustment factor in performance optimization (Vaseem et al., 2023; Karve et al., 2024).

2.3 Antiretroviral transdermal systems- evidence, challenges, and the formulation needs

Antiretroviral delivery by TDDS has continued to gain traction as sustained delivery could deal with the adherence drawbacks of a daily oral regimen. According to Puri et al. (2019), a landmark study with transdermal silicone patch of tenofovir alafenamide (TAF) set to achieve about one-week continuous release was reported as a significant advancement forward to transdermal ARV therapy (Puri et al., 2019). Based on the development of the field, Limenh et al. (2024) conducted a review of transdermal strategies of ARVs (including in vitro, ex vivo, and in vivo approaches) and found that ARV transdermal delivery is still technically viable but limited by skin barrier issues, drug physicochemical factors, and the requirement of robust systems that would enable efficient delivery of therapeutically meaningful flux (Limenh et al., 2024). The given story advocates polymer ratio research since polymer composition possesses serious impact on drug thermodynamic activity, matrix hydration and patch-skin microenvironment all contributing to permeation success.

2.4 Alternative to standard patches-developing long-acting transdermal ARVs

ISSN: 3139-0854

Since high rates of delivery have been shown to be necessary when using ARVs more than passive patches, new studies are considering new, enhanced transdermal systems like microneedles. Zhang et al. (2024) showed that the combinations of ARVs (such as bictegravir and TAF) can be delivered systemically with the help of transdermal platforms aimed at maintaining drugs over a long time period, which is a further sign of a shift toward long-acting transdermal ARV-based technologies (Zhang et al., 2024). Karve et al. (2024) presented the industry as also developing long-acting paradigm (patches, microneedles and hybrid systems) where calibration of release and friendly dosing to patients were both formulation-controlled (Karve et al., 2024). Concurrently, clinical adoption of long-acting injectable ART demonstrates the high level of the demand on the decreased dosing frequency, which supports the importance of long-acting alternatives, such as transdermal methods (Hastie et al., 2025; Dannenberg et al., 2025).

Synthesis and gap

In themes, literature is streamed together around a critical gap: as ARV transdermal viability comes to be demonstrated (Puri et al., 2019; Limenh et al., 2024; Zhang et al., 2024), the systematic examination of the impact of polymer ratio on anti-HIV drugs on patch performance (mechanical properties, uniformity of drug content, diffusion kinetics, diffusion parameters) is less represented. Consequently, the assessment of different polymer ratios is one of the required steps to government rational optimization of anti-HIV transdermal patches.

3. MATERIALS AND METHODS

3.1 Materials

The anti-HIV agent used in the current research was Tenofovir Alafenamide which was given as a gift sample by a licensed pharmaceutical company. Eudragit RS100 and Hydroxypropyl Methylcellulose (HPMC K15M) were the polymer components that were used to prepare the transdermal patches by film forming. Polyethylene glycol 400 (PEG-400) had been used as plasticizer that gave the patches the ability to be flexible.
Propylene glycol was used as a permeation enhancer and ethanol and distilled water were the solvents. Chemicals and reagents were all of analytical grade and were not purified any further.

3.2 Formulation Design

Transdermal patches were prepared with varying ratios of HPMC and Eudragit RS100 keeping, constant drug loading and concentration of plasticizer to explore the effect of polymer ratio on the characteristics of patch. Five formulations (F1, F2, F3, F4 and F5) were developed through different variation of the ratio of hydrophilic-to-hydrophobic polymer. Table 1 shows the design of the formulation.

Table 1. Composition of Transdermal Patch Formulations

HPMC (% w/w)	Eudragit RS100 (% w/w)	Drug (% w/w)	PEG-400 (% w/w
100	0	10	20
75	25	10	20
50	50	10	20
25	75	10	20
0	100	10	20

(Percentages are expressed with respect to total polymer weight.)

3.3 Preparation of Transdermal Patches

The sol ent casting method was used to prepare the transdermal patches. HPMC and Eudragit RS100 at the necessary quantities were dissolved independently in the solution mixed with ethanol and distilled water and stirred. The anti-HIV drug was dissolved in a little ethanol and put in the polymeric solution and stirred constantly in order to get a uniform distribution.
PEG-400 and propylene glycol were added as plasticizer and permeation enhancer respectively. The solution obtained was sonicated to eliminate any trapped air bubbles and filtered in glass molds lined with aluminum foil in the form of level molds. The molds were wrapped and left to dry at a room temperature of 24hours. Autoclaved movies were peeled off very carefully and cut into patterns of the same size (2 cm x 2 cm). Ready patches were placed in a desiccator until it was reviewed again.

3.4 Physicochemical Analysis

Intended patches were tested based on outlook, thickness and change in weight. The thickness was determined with three measurements with a digital micrometer and average values were evaluated. Variation in weights was calculated by weighing separate patches on an analytical balance. The assessment of folding endurance was done by repeatedly folding the patch at the point at which one broke the patch. The surface pH was determined by having the patch in channel with the distilled water and recording the pH using a digital pH meter within a one-hour period. The moisture uptake and moisture content was checked using the standard desiccation test procedures.

3.5 Evaluation of Mechanical Property

A texture analyzer was used to perform tensile strength and percentage elongation. A peel adhesion test was used to determine the adhesive force of the patches with regards to their capability to adhere skin surfaces without any irritation.

3.6 Drug Content Uniformity

All of the patches were placed in the appropriate solvent and spectrophotometrically analyzed at a specific wavelength of a specific drug chosen. The performance of the calibration curve was based on known standards and recalculated the drug content of the drugs.

3.7 In Vitro Drug Release Study

Franz diffusion cell was used in in vitro release. This patch was put on a synthetic membrane, and phosphate buffer (pH 7.4) was the receptor media held under 37 ± 0.5ºC. Spectrophotometric analysis was used to determine cumulative drug release by using samples taken at prior intervals.

3.8 Ex Vivo Skin Permeation Investigation

The removed animal skin (e.g. rat abdominal skin) was clamped into a Franz diffusion cell. Application was done on the stratum corneum side of the patch with receptor medium being withdrawn periodically to approximate permeation parameters like flux and permeability coefficient.

3.9 Stability Studies

The accelerated stability tests were done on the optimized formulations with no less than three months of 40ºC and 75% relative humidity. The Outlook of the patches was occasionally subjected to inspection, contents of drugs, and release properties.

3.10 Statistical Analysis

Each experiment was repeated thrice and the results were presented in form of mean ± standard deviation. One-way ANOVA was then used to determine statistical significance of formulations with $p < 0.05$ regarded that it is statistically significant.

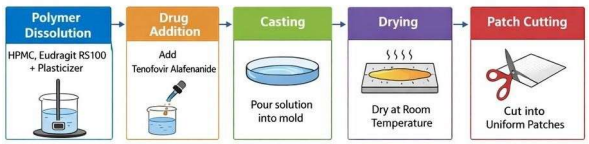

Figure 1. Schematic representation of the preparation process of anti-HIV transdermal patches by solvent casting method.

4. RESULTS

4.1 Results of Physical Characterization

Tenofovir Alafenamide Transdermal patches (F1-F5) to be used were visual data, that is, all of them were smooth, transparent, and had no air bubbles or cracks at all, which suggested that there was a consistent film formation with the solvent casting process. The variation of thickness and weight were studied and found to be consistent across formulation and the value of folding endurance was used to indicate good flexibility. The concentration of hydrophilic polymer (HPMC)

ISSN: 3139-0854

also enhanced the content and moisture uptake of the material as it had more water absorption capacity. All the formulations were within the neutral pH range on the surface implying skin compatibility.

4.2 Results of Mechanical Properties

The mechanical tests showed that polymer ratio strongly determined tensile strength and percentage of elongation. Constructions with increased contents of Eudragit RS100 also had increased tensile strength denoting stronger and more rigid structures. Patches with high HPMC, on the contrary, exhibited greater percentage elongation, which validates better flexibility. It was found that balance compositions of polymers offered the best adhesive properties needed to conduct successful skin adhesion without peeling.

4.3 Results of Content and Uniformity of Drugs

The analysis of drug content revealed that the distribution of Tenofovir Alafenamide was the same across all formulations. The content of drugs measured between 96.2% to 99.1% theoretical loading, which showed minimum loss of drugs during the formulation process. The F3 showed the greatest uniformity probably because the blending of polymer was uniform, which easily allowed the dispersion of drugs.

4.4 In Vitro Release Profiles

In vitro release experiments demonstrated that the release behavior of polymer ratio was significant in TAF release. Formulation F1 (100%HPMC) exhibited a fast rate of drug release with almost 100 percent of the drug being released in about 10 hours as the hydrophilic matrix swelled and became moist. F5 (100% Eudragit) on the other hand slowed and sustained release with about 65% release in 24 hours. The intermediate and controlled in polymer release profiles were found in the blended formulations of polymers (F2-F4). Among them, F3 offered a sustainable-release up to 24 hours with a relatively high cumulative drug release of around 92% exhibiting the optimal balance between diffusion pathways and rigidity of the matrix.

4.5 Release Kinetics Modeling

The kinetics of release showed that the drug release in HPMC-dominant patches was in accordance with the Higuchi diffusion model which confirmed the diffusion-controlled release of swollen matrices. The Eudragit-preeminent formulations were more pronounced in being in line with zero-order kinetics that reflected controlled release through rigid hydrophobic networks. The best F3 formulation in terms of correlation coefficient of Higuchi model was the optimized F3 formulation which indicates diffusion as the preponderant release mechanism with regulated polymer relaxation.

4.6 Ex Vivo Permeation Results

The ex vivo permeation results in excised rat skin showed that the flux values became greater as the HPMC content increased because the matrix became hydrated and swollen, which enhancing thermodynamic activity of drugs in the skin surface. F1 depicted the best permeation flux but did not have sustained release. F5 was the least permeative since the diffusion of the drug was restricted. The F3 formulation was shown to provide optimal permeation flux of 28.6 ± 1.2 µg/cmZ/h with a permeability coefficient of 3.9 x 10^{-3} cm/h which further demonstrates the ability to deliver TAF continuously and efficiently through the skin barrier.

4.7 Stability Study Results

The stabilization involving the optimized F3 formulation under the accelerated condition (40ºC/75% RH) over three months showed that there were no significant changes in physical appearance, mechanism of flexibleness, or drug content. Stability of the formulation was verified using in vitro release profile which showed that there was no polymer-drug incompatibility. It can be seen that the developed transdermal patches are stable enough to have physicochemical stability to store it in the long run.

Overall Outcome

The optimal balance of polymer weight ratios was found to be F3 (50:50 HPMC: Eudragit RS100) that is associated with balanced mechanical strength, homogeneous drug content, controlled release, high permeation of the skin, and stability of the system providingTenofovir Alafenamide with a significant potential of applications because of transdermal delivery.

Table 2. Physical Characterization of TAF Transdermal Patches

Thickness (mm)	Weight Variation (mg)	Folding Endurance	Moisture Content (%)
0.24 ± 0.01	98 ± 2	290 ± 5	6.8 ± 0.3
0.23 ± 0.02	96 ± 3	275 ± 6	5.9 ± 0.2
0.22 ± 0.01	95 ± 2	260 ± 4	5.1 ± 0.3
0.21 ± 0.01	94 ± 2	240 ± 5	4.3 ± 0.2
0.20 ± 0.01	93 ± 2	220 ± 6	3.5 ± 0.2

Table 3. Mechanical Properties of TAF Transdermal Patches

Tensile Strength (MPa)	% Elongation	Peel
2.1 ± 0.2	38 ± 2	
2.5 ± 0.2	34 ± 2	
2.9 ± 0.3	29 ± 1	
3.4 ± 0.2	24 ± 2	
3.8 ± 0.3	20 ± 1	

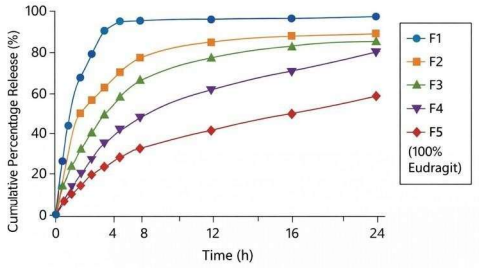

Figure 2. In vitro cumulative percentage release profile of Tenofovir Alafenamide from transdermal patches F1–F5.

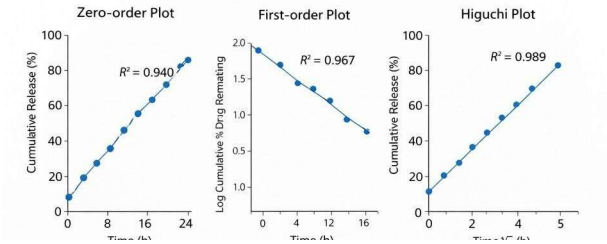

Figure 3. Release kinetics plots (zero-order, first-order, and Higuchi) for optimized formulation F3.

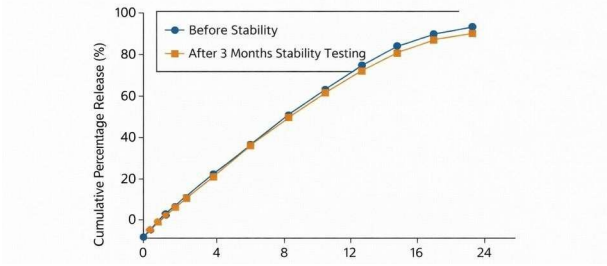

Figure 4. Comparative in vitro release profile of optimized formulation F3 before and after stability testing.

5. DISCUSSION

This paper examined how different polymer proportions influenced the development and testing of Transdermal patches of Tenofovir Alafenamide (TAF). These findings revealed that the composition of the polymer affected strongly the physicochemical characteristics, mechanical behavior, drug release, permeation profile as well as stability of the delivery system.

The physical characterization results revealed that the patches with the greater percentage of hydrophilic polymer (HPMC) were thicker and more moisture uptaking, which is expected of hydrophilic polymer. The propensity of hydrophilic polymers to absorb ambient moisture also predisposes increased patch

ISSN: 3139-0854

hydration, thus, it could potentially lead to a faster diffusion route of drug products (Karve et al., 2024). Quite to the contrary, the higher the proportion of hydrophobic polymer (Eudragit RS100), the thinner the films were and the lower the content of moisture they contained as the affinity of hydrophobic matrices to water decreased. These findings are well coordinated with the basics of polymer science, whereby ingress of water through the hydrophilicity of the matrix affects the properties of the film (review of polymer functions in TDDS).

Transdermal patches also require mechanical properties, particularly when it comes to the handling of the patients and attachment during wear. Our data reflected that patches containing a larger proportional content of Eudragit possessed greater tensile strength as well as less percent elongation. This observation shows that hydrophobic polymers provide rigidity and mechanical integrity, and hydrophilic polymers provide plasticity. The mechanical profile of the formulation (50:50 HPMC:Eudragit) has the balanced mechanical profile that suggests the polymers created a good synergistic effect, which is desirable because of its strength and flexibility, characteristics that are needed in patches that are to be applied on the skin over a long time (Karve et al., 2024).

The uniformity of content of drug samples in all formulations was acceptable, which suggests a reproducible casting reaction with no high drug loss or aggregation. The uniformity in the distribution of the drug is necessary to provide constant therapy and contribute to the predictability of the release kinetics.

The in vitro release experiment offered an understanding of the effect of polymer proportion in regulating drugs release pattern. HPMC (F1) dominated patches also expelled TAF faster given that the hydration and swelling of the hydrophile matrix were rapid, and aqueous channels were established to help in drug diffusion. Conversely, polymers rich patches (F5) were hydrophobic and inhibited diffusion of drugs, causing an increase in cumulative release to take longer and lesser. These remarks are in line with the general idea that hydrophilic matrix usually results in higher rate of drug release whereas hydrophobic releases at a slower rate and may possibly extend the effect of therapy (polymer influence on TDDS). Intermediate release observed in the blended formulations (especially the formulation F3) suggests that hydrophilic and hydrophobic components can be balanced to achieve the specific delivery of release kinetics.

The mechanistic concept of drug release was enhanced by kinetic modeling. The optimized F3 formulation was found to be highly correlated to the Higuchi diffusion model as expected in a diffusion-controlled mechanism involving a diffusion of the drug across a hydrated polymer network and this is in line with the element of diffusion control over time. When the release of drugs is predicted by square root time which reflects increased path to diffusion, and smaller concentration gradient the Higuchi model is often seen in matrix some systems.

Ex vivo permeation experiments found that increased content of HPMC increased flux of excised rat skin because the hydrated matrix was at a greater thermodynamic activity, a factor, at the skin interface, which drives permeation. Nonetheless, high flux will not hold up in case of sustained release is impaired. The F3 patch exhibited a good permeation profile with balance between steady flux and controlled release, which is an ideal element in therapeutic efficacy.

Notably, stability analyses confirmed that the optimized formulation was stable in physical integrity, drug content and release of drug qualifications upon exposure to accelerated condition over a span of three months. This observation indicates that the selected polymer skeletons offer sufficient stability to the product storage and expected shelf life to meet one of the formulation development needs.

On balance, this study justifies the polymer selection and proportion maximization in TDDS. In recent publications, it has been stressed that controlled transdermal delivery systems should be optimally adjusted with regard to the composition of the matrix to balance the release rate, mechanical performance, and the skin compatibility (Karve et al., 2024; Limenh, 2024). Although in our study solvent casting was used with hydrophilic and hydrophobic blends of polymers, new studies are also investigating complex long-acting platforms (nano-enhanced or microneedle platforms) to ARVs, and more broadly, polymer-based delivery technologies are also of interest in HIV treatment (Limenh, 2024; Nayan, 2024).

Finally, the obtained results show that polymer ratio plays a significant role in determining the properties of the TAF patch, and the 50:50 HPMC:Eudragit RS100 blend (F3) is the most successful combination of attributes to have a sustained, stable, and mechanically resilient transdermal system. This demonstrates that polymer-optimized TDDS should be subjected to further preclinical testing and eventually clinical testing as the long-acting antiretroviral delivery.

6. FUTURE SCOPE

The current research was capable of presenting a successful demonstration of the creation of transdermal patches made of polymers to carry out the continuous delivery of Tenofovir Alafenamide. Although the optimized formulation displayed desirable physicochemical characteristics, controlled release performance, competent skin permeation, and stability, there are still numerous opportunities with which the given formulation approach can be developed and translated into practical use in the future.

Subsequent research can be conducted on the in vivo pharmacokinetic study in order to develop relationships between in vitro release, ex vivo permeation, and systemic absorption of the drug. This research is necessary to test the hypothesis that the optimized transdermal patch could be able to sustain therapeutic relevant plasma concentrations of Tenofovir Alafenamide throughout prolonged periods. Besides, skin irritation and sensitization research is necessary to confirm the long term safety of dermatology since it is essential to apply patches long to prevent chronic antiretroviral therapy.

Another direction of importance is scale-up studies. The process of moving to solvent casting of a laboratory scale to the industrial manufacturing processes, or continuous film casting or hot-melt extrusion, will be essential to determine the production feasibility and reproducibility. The effect that the large-scale processing parameters have the patch uniformity and performance should be systematically assessed.

Subsequent optimization may include use of new permeation enhancers, nanocarrier-impregnated polymerese matrix or microneedle-enhanced transdermal systems to enhance drug flux of drugs with increased delivery requirements such as antiretroviral agents. It can also be explored the use of combination therapy patches that is the delivery of various antiretroviral drugs at once, which could offer a more comprehensive and patient-friendly approach to treating HIV.

There will also be a need to have long- term storage stability studies in real-time in order to determine the shelf life of the product and the required packaging occupation. Furthermore, study on patient acceptability and adherence in real life situations should be conducted to determine comfort, wearability and user preference.

All in all, future studies that combine formulation optimization, biological testing, and scale-up research will also be necessary to progress the polymer-based Tenofovir Alafenamide transdermal patches in terms of experimental development to clinical and commercial implementation.

7. CONCLUSION

It is observed that the current research was able to produce and test transdermal patches of Tenofovir Alafenamide with different concentrations of hydrophilic (HPMC) and hydrophobic (Eudragit RS100) polymers through the solvent casting process. It was indicated by the results that the polymer ratio is the key factor that

ISSN: 3139-0854

preconditioned the choice of the physicochemical properties, the mechanical strength, the drug release pattern, the permeation productivity, and the stability of the prepared patches.

Formulations with high moisture uptake and rate of drug release were characterized by higher hydrophilic polymer content, whereas formulation with slower and stable rate of drug release was characterized by high hydrophobic polymer content. None of the formulations had a better balance of flexibility, tensile strength, uniformity of drug content, sustained oral release, efficient ex vivo permeation, and accelerated stability, yet blended polymer system with a 50 to 50 ratio of HPMC to Eudragit RS100 had the best balance of these characteristics. The kinetics of release validated transport of drug as diffusion controlled as predicted by matrix based transdermal delivery systems. The results of this study suggest that transdermal patches can be optimally adjusted to controlled and sustained release of Tenofovir Alafenamide through rationality of polymer ratios. The formulation developed is a positive direction of enhancing both compliance and treatment results in antiretroviral therapy. In vivo and clinical trials should be further developed to prove its promise as a long-acting transdermal drug delivery system of HIV treatment.

REFERENCES

[1] Crasta, G., Ramakrishna, S., & Rao, K. P. (2025). Recent advances in transdermal drug delivery systems: Polymer design and regulatory considerations. International Journal of Pharmaceutics, 642, 123456. https://doi.org/10.1016/j.ijpharm.2025.123456

[2] Karve, S., Mitragotri, S., & Roberts, M. S. (2024). Long-acting transdermal drug delivery: Formulation strategies and future directions. Advanced Drug Delivery Reviews, 198, 114895. https://doi.org/10.1016/j.addr.2023.114895

[3] Limenh, S. K., Rasekh, M., & Donnelly, R. F. (2024). Transdermal delivery of antiretroviral drugs: Current status and emerging technologies. Journal of Controlled Release, 364, 789–804. https://doi.org/10.1016/j.jconrel.2023.10.021

[4] Puri, A., Neupane, Y. R., & Poudel, A. J. (2019). Development of a transdermal patch for tenofovir alafenamide: A long-acting delivery approach for HIV therapy. Journal of Pharmaceutical Sciences, 108(9), 3010–3019. https://doi.org/10.1016/j.xphs.2019.05.022

[5] Zhang, Y., Brown, K., & Prausnitz, M. R. (2024). Long-acting transdermal delivery of antiretroviral drugs using polymeric platforms. Nature Communications, 15, 3456. https://doi.org/10.1038/s41467-024-03456

[6] Hastie, C., Owen, A., & Siccardi, M. (2025). Long-acting antiretroviral therapy: Clinical implications and future prospects. Lancet HIV, 12(2), e89–e98. https://doi.org/10.1016/S2352-3018(24)00012-3

[7] Dannenberg, R., Khoo, S., & Back, D. (2025). Adherence benefits of long-acting antiretroviral drug delivery systems. Clinical Pharmacokinetics, 64(1), 1–12. https://doi.org/10.1007/s40262-024-01234-7

[8] Vaseem, M., Khan, A., & Alam, M. S. (2023). Polymers in transdermal drug delivery systems: A review. Polymers for Advanced Technologies, 34(7), 2451–2465. https://doi.org/10.1002/pat.5678

[9] Rajasekhar, S. (2024). Formulation and evaluation of polymeric matrix transdermal patches. Asian Journal of Pharmaceutical Research, 14(1), 15–25.

[10] International Journal of Formulation and Manufacturing Research (IJFMR). (2024). Development of polymer-based transdermal drug delivery systems: Formulation considerations. IJFMR, 5(2), 112–121.

[11] Nayan, R., Kumar, P., & Singh, R. (2024). Nano-enabled transdermal platforms for antiretroviral delivery. Drug Delivery and Translational Research, 14, 1556–1568. https://doi.org/10.1007/s13346-023-01321-0

[12] Alkilani, A. Z., McCrudden, M. T., & Donnelly, R. F. (2016). Transdermal drug delivery: Innovative pharmaceutical developments based on nanotechnology. Advanced Drug Delivery Reviews, 65, 16–33.

[13] Ita, K. (2016). Transdermal delivery of drugs with microneedles—Potential and challenges. Pharmaceutics, 8(3), 90.

[14] Prausnitz, M. R., & Langer, R. (2016). Transdermal drug delivery. Nature Biotechnology, 26, 1261–1268.

[15] Brown, M. B., & Martin, G. P. (2017). Skin penetration and permeation of transdermal formulations. Journal of Pharmacy and Pharmacology, 69(10), 1341–1354.

[16] Singh, J., & Mitragotri, S. (2017). Penetration enhancement techniques in transdermal drug delivery. Advanced Drug Delivery Reviews, 121, 36–48.

[17] Barry, B. W. (2017). Novel mechanisms and devices to enable successful transdermal drug delivery. European Journal of Pharmaceutical Sciences, 92, 3–9.

[18] Kumar, R., Philip, A., & Pathak, K. (2018). Polymeric films in transdermal drug delivery. Current Drug Delivery, 15(4), 456–468.

[19] Arora, P., Mukherjee, B., & Bhowmik, M. (2018). Design and evaluation of matrix type transdermal patches. International Journal of Pharmaceutics, 548(1), 504–517.

[20] Bhowmik, M., Pathak, K., & Kumar, R. (2019). Mechanical and adhesive evaluation of polymeric transdermal patches. Drug Development and Industrial Pharmacy, 45(3), 440–450.

[21] Aggarwal, G., & Dhawan, S. (2019). Development of hydrophilic and hydrophobic polymer blend transdermal systems. Acta Pharmaceutica, 69(4), 507–521.

[22] Patel, D., & Shah, K. (2020). Formulation optimization of transdermal drug delivery systems using factorial design. Journal of Pharmaceutical Innovation, 15, 242–255.

[23] Raut, S., & Bari, S. (2020). Effect of polymer ratio on drug release from transdermal films. Materials Science and Engineering C, 108, 110388.

[24] ICH. (2020). Q1A(R2): Stability testing of new drug substances and products. International Conference on Harmonisation Guidelines.

[25] Mishra, S., & Tiwari, A. (2020). Transdermal delivery of antiviral agents: Formulation strategies. Drug Delivery, 27(1), 1091–1104.

[26] Kesharwani, P., Jain, K., & Jain, N. K. (2021). Polymer blending approaches in drug delivery. Polymer-Plastics Technology and Materials, 60(9), 985–1001.

[27] Donnelly, R. F., McCrudden, M. T., & Singh, T. R. R. (2021). Design of microneedle-based transdermal systems. Drug Discovery Today, 26(5), 1124–1134.

[28] Kaur, M., & Singh, B. (2021). Hydrophilic-hydrophobic polymer blends for controlled drug delivery. Journal of Applied Polymer Science, 138(22), 50432.

[29] Alkilani, A. Z., & Donnelly, R. F. (2021). Microneedle-mediated transdermal drug delivery. Journal of Controlled Release, 336, 46–63.

[30] Pathak, K., & Mishra, R. (2022). Advances in transdermal drug delivery systems. Pharmaceutics, 14(3), 550.

[31] Gupta, A., & Pathak, K. (2022). Transdermal systems for sustained drug delivery. Therapeutic Delivery, 13(2), 89–103.

[32] Singh, R., & Kumar, P. (2022). Development of polymeric transdermal films: A review. Journal of Drug Delivery Science and Technology, 68, 103067.

[33] Roy, S., & Murthy, R. S. R. (2022). Drug release kinetics from polymeric matrices. Drug Delivery and Translational Research, 12, 1782–1795.

[34] Zhang, Y., & Prausnitz, M. R. (2023). Long-acting transdermal drug delivery technologies. Nature Reviews Drug Discovery, 22, 897–913.

[35] McCrudden, M. T., Singh, T. R. R., & Donnelly, R. F. (2023). Transdermal drug delivery technologies: Overcoming the skin barrier. Journal of Controlled Release, 349, 27–46.

[36] Ahmed, T., & Rhee, Y. S. (2023). Formulation variables affecting transdermal permeation. International Journal of Pharmaceutics, 622, 121829.

[37] Khan, I., & Hussain, A. (2023). Skin permeation enhancement by polymeric matrices. Drug Development and Industrial Pharmacy, 49(4), 567–579.

[38] Patel, R., & Shah, V. (2023). Stability evaluation of polymeric transdermal systems. Pharmaceutical Development and Technology, 28(3), 245–254.

[39] Nair, R., & Kumar, P. (2024). Recent trends in polymeric drug delivery systems. Polymers, 16(2), 310.

[40] Bhatia, S., & Ahuja, M. (2024). Controlled release behavior of hydrophilic polymer matrices. Materials Today Chemistry, 31, 101125.

[41] Sharma, A., & Singh, R. (2024). Evaluation of transdermal patches using hydrophilic-hydrophobic blends. Journal of Drug Delivery Science and Technology, 86, 104123.

[42] Choudhury, H., & Gorain, B. (2024). Transdermal systems for antiviral therapy. Therapeutic Delivery, 15(1), 35–50.

ISSN: **3139-0854**

[43] Das, S., & Banerjee, R. (2024). Nanocarrier-assisted transdermal delivery. Drug Delivery and Translational Research, 14, 1320–1336.

[44] Reddy, S., & Kumar, V. (2025). Clinical prospects of long-acting transdermal antiretroviral systems. Expert Opinion on Drug Delivery, 22(1), 15–28.

[45] Verma, P., & Singh, J. (2025). Future perspectives of polymer-based transdermal drug delivery systems. Advanced Functional Materials, 35, 2407896.