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Development and Optimization of Local Anesthetic Lidocaine Transdermal Films Using Solvent Casting Technique

Mrs. M. Shravani^{1*}, Ms. K. Pranitha²

¹Assistant Professor, Department of Pharmaceutics, KVK College of Pharmacy, Surmaiguda, Laskarguda, Abdullapurmet, Hyderabad, Telangana (St), India.

²Post Graduate Pharmacy Scholar, KVK College of Pharmacy, Surmaiguda, Laskarguda, Abdullapurmet, Hyderabad, Telangana (St), India.

Corresponding Author: Mrs. M. Shravani

Email id : shravani.pharmacy21@gmail.com



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Abstract: The present study was aimed at the development and characterization of polymeric transdermal patches of lidocaine for sustained drug delivery to provide prolonged therapeutic action, improve patient compliance, and reduce the frequency of drug administration. Lidocaine-loaded transdermal patches were prepared by the solvent casting method using Hydroxypropyl Methylcellulose (HPMC) and Sodium Alginate as film-forming polymers. Polyethylene glycol (PEG) was incorporated as a plasticizer, while D-limonene was used as a permeation enhancer. Eight formulations (F1–F8) were developed by varying the polymer concentration to optimize the formulation characteristics. The prepared patches were evaluated for physicochemical parameters including weight variation, thickness, folding endurance, drug content, percentage moisture loss, and percentage moisture absorption. The patches exhibited satisfactory physical appearance, uniform thickness, good flexibility, and acceptable mechanical strength. Drug content ranged from 79.53% to 93.56%, with formulation F8 showing the highest drug content (93.56%). In vitro drug release studies carried out using a Franz diffusion cell demonstrated sustained drug release over a period of 12 hours. Among all formulations, F4 exhibited the highest cumulative drug release (98.88%), while the optimized formulation F8 achieved 98.35% cumulative drug release with superior overall physicochemical characteristics. Drug release kinetic analysis of formulation F8 showed the best fit to the Higuchi model ($R^2 = 0.973$), indicating diffusion-controlled drug release through the hydrated polymeric matrix. Accelerated stability studies of the optimized formulation were conducted at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity for three months. The formulation remained stable, showing only negligible changes in drug content, folding endurance, physical appearance, and cumulative drug release, confirming its satisfactory physical and chemical stability. The findings of the present investigation demonstrate that the developed polymeric transdermal patches are capable of delivering lidocaine in a sustained and controlled manner. The optimized formulation exhibited excellent physicochemical properties, prolonged drug release, and good stability, indicating its potential as an effective transdermal drug delivery system for long-term pain management. Further ex vivo and in vivo studies are recommended to establish its clinical efficacy and therapeutic performance.

Key words. Lidocaine, Hydroxypropyl Methylcellulose, Polyethylene glycol, transdermal patches

INTRODUCTION

TRANSDERMAL PATCHES

Transdermal drug delivery systems (TDDS), commonly known as transdermal patches, are advanced pharmaceutical dosage forms designed to deliver drugs through the skin into the systemic circulation at a controlled and predetermined rate. These patches provide a non-invasive alternative to conventional oral and injectable drug delivery systems by allowing the drug to penetrate the skin and enter the bloodstream without passing through the gastrointestinal tract or undergoing first-pass hepatic metabolism. The skin, particularly the stratum corneum, acts as a protective barrier; however, suitable drug molecules with appropriate physicochemical properties can successfully diffuse across this barrier when formulated with suitable polymers, permeation enhancers, and adhesives.

The success of transdermal drug delivery depends largely on the physicochemical properties of the drug. Ideal candidates for transdermal administration generally possess low molecular weight (less than 500 Da), adequate lipophilicity (log P between 1 and 3), low daily dose requirements, and sufficient potency. Drugs such as nitroglycerin, nicotine, fentanyl, clonidine, lidocaine, rivastigmine, and estradiol have been successfully formulated as transdermal patches and are widely used in clinical practice.

Advantages

1. **Avoids First-Pass Metabolism:** Drugs are absorbed directly into the systemic circulation, bypassing hepatic first-pass metabolism and improving bioavailability.
2. **Controlled and Sustained Drug Release:** Provides continuous drug delivery over an extended period, maintaining consistent plasma drug concentrations.
3. **Improved Patient Compliance:** Easy to apply, painless, and convenient, making them suitable for long-term therapy.
4. **Reduced Dosing Frequency:** Sustained drug release minimizes the need for frequent administration.
5. **Non-Invasive Delivery:** Eliminates the pain and discomfort associated with injections.
6. **Easy Termination of Therapy:** Drug administration can be stopped immediately by removing the patch if adverse effects occur.

Disadvantages

1. **Limited Drug Selection:** Only drugs with suitable molecular weight, lipophilicity, and potency can be effectively delivered through the skin.
2. **Skin Irritation:** Prolonged application may cause erythema, itching, allergic reactions, or contact dermatitis.
3. **Limited Drug Loading Capacity:** High-dose drugs are generally unsuitable due to limited patch size and skin permeability.
4. **Poor Permeability of Hydrophilic Drugs:** The stratum corneum significantly restricts the permeation of water-soluble and large molecules.
5. **Variability in Skin Permeability:** Drug absorption may vary depending on age, skin condition, hydration, temperature, and application site.
6. **Adhesion Problems:** Poor adhesion due to sweating, body movement, or moisture may reduce therapeutic effectiveness.

MATERIALS AND METHODS

MATERIALS:

Lidocaine were obtained as pure sample from Aurobindo Ltd, HYD., as gift samples along with their analytical reports. Sodium alginate, HPMC K15M was obtained from SD Fine Chemicals, Mumbai, PEG

400 was obtained from S. D. Fine Chem. Ltd., Mumbai. All other chemical were purchased from Hi Media, Mumbai. Double distilled water was prepared freshly and used whenever required. All other chemicals used in this study including those stated were of analytical reagent (A.R.) grade.

METHODOLOGY

PREFORMULATION STUDIES

Methods of API characterization

Physical appearance

The physical appearance of Lidocaine was evaluated by visual inspection under normal daylight conditions. A small quantity of the drug sample was placed on a clean, dry white porcelain tile or watch glass and examined for its color, odor, appearance, texture, and physical state. The sample was observed for the presence of any visible impurities, discoloration, or foreign particulate matter. The organoleptic characteristics were recorded and compared with the standard specifications reported in the official pharmacopeia or literature to confirm the identity and purity of the drug. The evaluation was performed in triplicate, and the observations were recorded as the average result.

Solubility Studies

The solubility of Lidocaine was determined in different solvents, including distilled water, phosphate buffer (pH 7.4), methanol, ethanol, acetone, and chloroform. An excess amount of lidocaine was added separately to 10 mL of each solvent in clean, tightly closed glass vials. The vials were shaken using a mechanical shaker at $25 \pm 2^\circ\text{C}$ for 24 hours to attain equilibrium. After equilibration, the samples were allowed to stand for 2 hours and then filtered through Whatman No. 1 filter paper to remove any undissolved drug. The filtrates were suitably diluted with the corresponding solvent, and the concentration of dissolved lidocaine was determined using a UV-Visible spectrophotometer at its respective λ_{max} . The solubility was expressed as mg/mL, and the study was performed in triplicate to obtain the mean value.

Determination of Melting Point

The melting point of Lidocaine was determined by the capillary tube method. A small quantity of finely powdered lidocaine was filled into a thin-walled capillary tube sealed at one end. The packed capillary tube was attached to a thermometer and placed in a melting point apparatus. The temperature was increased gradually at a rate of $1-2^\circ\text{C}$ per minute near the expected melting range. The temperature at which the drug started to melt and the temperature at which it was completely liquefied were recorded. The melting point determination was carried out in triplicate, and the average melting point was calculated. The observed melting point was compared with the reported literature value to confirm the purity and identity of the drug.

Preparation of phosphate buffer pH 7.4:

2.48 gm of di- sodium hydrogen orthophosphate and 0.19 gm of potassium dihydrogen phosphate and 8gm of sodium hydroxide was weighed to it sufficient water was added to get 1000 ml and the pH was altered to 7.4 with Ortho phosphoric acid.

Standard curves of Lidocaine:

Standard graph of Lidocaine in phosphate buffer 7.4:

10 mg of drug was dissolved in 10 ml of PBS (phosphate buffer saline, pH 7.4) and diluted with distilled water up to 100ml. 1ml sample of the solution was diluted up to 10 ml with 10% v/v PBS solution. After the dilution the solution was examined in the UV spectrophotometer (UV-1800, Shimadzu, Tokyo, Japan) between 200 nm to 400 nm. The UV spectra of the drug was recorded and compared with reported absorption maximum

Fourier transform infrared spectroscopy (FTIR) analysis

Approximately 1–2 mg of the finely powdered sample was accurately weighed and mixed thoroughly with 100–200 mg of dry, IR-grade potassium bromide (KBr). The mixture was triturated uniformly in an agate mortar to obtain a fine powder and then compressed under hydraulic pressure to form a transparent pellet. The prepared KBr pellet was placed in the sample holder of the FTIR spectrophotometer. The infrared spectra were recorded over the wavelength range of $4000-400\text{ cm}^{-1}$ with an appropriate spectral resolution

(typically 4 cm^{-1}) and the required number of scans. The spectra of the pure drug, polymers, and the optimized transdermal patch formulation were compared to identify the characteristic absorption peaks corresponding to the functional groups of lidocaine. The obtained spectra were analyzed for any appearance, disappearance, broadening, or shifting of characteristic peaks. The absence of significant changes in the characteristic peaks indicated good compatibility between Lidocaine and the selected excipients, confirming that no chemical interaction had occurred during formulation development.

Formulation design

Table 1: Formulation Design of Lidocaine Transdermal Patches

FORMULATION CODE	DRUG (mg)	HPMC (mg)	SODIUM ALGINATE (mg)	PEG (ml)	D-LIMONENE (ml)
F1	100	100	-	1	0.1
F2	100	200	-	1	0.1
F3	100	300	-	1	0.1
F4	100	400	-	1	0.1
F5	100	-	100	1	0.1
F6	100	-	200	1	0.1
F7	100	-	300	1	0.1
F8	100	-	400	1	0.1

Preparation of Lidocaine Polymeric Transdermal Patches (Solvent Casting Method)

Initially, the required quantity of HPMC (for formulations F1–F4) or Sodium Alginate (for formulations F5–F8) was accurately weighed according to the formulation design and dispersed separately in an appropriate quantity of distilled water. The polymer solution was stirred continuously using a magnetic stirrer until a clear and homogeneous viscous solution was obtained. The solution was then allowed to stand for approximately 30 minutes to ensure complete hydration of the polymer and to eliminate entrapped air bubbles.

Separately, 100 mg of Lidocaine was accurately weighed and dissolved in a small quantity of a suitable solvent such as ethanol or a hydroalcoholic mixture to obtain a clear drug solution. The drug solution was slowly added to the hydrated polymer solution under continuous stirring to ensure uniform distribution of the drug throughout the polymeric matrix.

After complete incorporation of the drug, 1 mL of polyethylene glycol (PEG) was added as a plasticizer to improve the flexibility and mechanical strength of the film. Subsequently, 0.1 mL of D-limonene was incorporated into the formulation as a permeation enhancer to improve transdermal drug permeation through the skin. The resulting mixture was stirred continuously until a smooth, homogeneous, and bubble-free casting solution was obtained.

The prepared casting solution was poured carefully into a clean, leveled glass Petri dish or Teflon-coated mould of known surface area. The solution was spread uniformly to obtain films of consistent thickness. The films were allowed to dry at room temperature for 24 hours or in a hot air oven maintained at $40 \pm 2^\circ\text{C}$ until complete evaporation of the solvent.

After drying, the formed polymeric films were carefully peeled from the casting surface and inspected visually for uniformity and the absence of defects such as cracks or air bubbles. The films were then cut into patches of the required dimensions, each containing the desired dose of lidocaine.

Finally, the prepared transdermal patches were wrapped individually in aluminum foil, packed in airtight containers, and stored in a desiccator until further evaluation. The patches were subsequently evaluated for physicochemical properties such as thickness, weight variation, folding endurance, moisture content, moisture uptake, tensile strength, drug content, surface pH, in vitro drug release, ex vivo skin permeation, and stability studies.

Evaluation of transdermal formulation:

Thickness

The thickness of the prepared transdermal patches was determined using a **digital micrometer screw gauge**. Each patch was measured at **three different locations** (center and two opposite edges) to ensure uniformity. The measurements were recorded in **millimeters (mm)**, and the average thickness with standard deviation was calculated for each formulation.

2. Folding Endurance

The folding endurance of the transdermal patches was determined manually by repeatedly folding the same patch at the same place until it broke or showed visible cracks. The number of times the patch could be folded without breaking was recorded as the **folding endurance**. The test was performed in triplicate, and the average value was calculated.

3. Weight Variation

Individual patches of equal dimensions were cut from different portions of each formulation. Each patch was weighed separately using a **digital analytical balance**, and the individual weights were recorded. The average weight and standard deviation were calculated to assess the uniformity of weight among the prepared patches.

4. Drug Content Uniformity

A transdermal patch of known area was accurately weighed and cut into small pieces. The pieces were transferred into a **100 mL volumetric flask** containing a suitable solvent, such as **phosphate buffer (pH 7.4) containing methanol**, to extract the drug completely. The solution was sonicated for **30 minutes** with intermittent shaking to ensure complete extraction of lidocaine. The resulting solution was filtered through **Whatman No. 1 filter paper**, suitably diluted, and analyzed using a **UV-Visible spectrophotometer** at the predetermined λ_{max} of lidocaine. The drug content was calculated as the percentage of the theoretical drug content, and the test was performed in triplicate.

5. Percentage Moisture Absorption

The prepared patches were accurately weighed (W_1) and placed in a desiccator containing a **saturated solution of potassium chloride (KCl)**, which maintained a relative humidity of approximately **84% RH**, at room temperature for **24 hours**. After the specified period, the patches were removed and reweighed (W_2). The percentage moisture absorption was calculated using the following equation:

$$\text{Moisture Absorption} = \frac{W_2 - W_1}{W_1} \times 100$$

where:

- W_1 = Initial weight of the patch
- W_2 = Final weight after moisture absorption

6. Percentage Moisture Loss

The prepared patches were weighed accurately (W_1) and placed in a desiccator containing **anhydrous calcium chloride** as a desiccant for **24 hours** at room temperature. After the specified period, the patches were removed and weighed again (W_2). The percentage moisture loss was calculated using the following equation:

$$\text{Moisture Loss} = \frac{W_1 - W_2}{W_1} \times 100$$

where:

- W_1 = Initial weight of the patch
- W_2 = Final weight after drying

In-vitro Drug Release Studies

The **in-vitro drug release study** of the lidocaine transdermal patches was carried out using a **Franz diffusion cell**. A dialysis membrane (previously soaked in phosphate buffer pH 7.4 for 12 hours) was mounted between the donor and receptor compartments. The receptor compartment was filled with **phosphate buffer (pH 7.4)**, maintained at $37 \pm 0.5^\circ\text{C}$, and stirred continuously using a magnetic stirrer at **50 rpm**.

A transdermal patch of known area was placed on the donor side of the membrane with the drug-loaded surface facing the membrane. At predetermined time intervals (0.5, 1, 2, 4, 6, 8, 10, and 12 hours),

5 mL of the receptor medium was withdrawn and immediately replaced with an equal volume of fresh phosphate buffer maintained at the same temperature to maintain sink conditions. The withdrawn samples were filtered if necessary, suitably diluted, and analyzed using a **UV-Visible spectrophotometer** at the λ_{max} of lidocaine. The cumulative percentage drug release was calculated and plotted against time.

Kinetic Modeling of Dissolution Data

The **in-vitro drug release data** obtained from the optimized formulation were fitted into various kinetic models, including **Zero-order, First-order, Higuchi, and Korsmeyer-Peppas** models, to determine the mechanism of drug release.

The cumulative percentage drug release data were transformed according to the mathematical equations of each kinetic model, and regression analysis was performed. The model showing the **highest correlation coefficient (R^2)** was considered the best fit for describing the drug release mechanism from the transdermal patches.

Stability Studies of Optimized Formulation

The optimized lidocaine transdermal patch formulation was subjected to accelerated stability studies according to **ICH Q1A(R2) guidelines**. The patches were individually wrapped in aluminum foil, sealed in laminated pouches, and stored in a stability chamber maintained at **$40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity** for a period of **3 months**.

Samples were withdrawn initially and after **1, 2, and 3 months** of storage. The stored patches were evaluated for physical appearance, thickness, folding endurance, drug content, moisture content, and **in-vitro drug release**. The results obtained after storage were compared with the initial values to assess the physical stability, chemical stability, and sustained drug release performance of the optimized formulation. The absence of significant changes in these parameters indicated that the transdermal patches remained stable throughout the storage period.

RESULTS & DISCUSSION

Preformulation studies

Solubility: Slightly soluble in water Freely soluble in alcohol and chloroform; slightly soluble in water

Determination of λ_{max} using UV- Visible spectrophotometer:

Lidocaine exhibits absorption maxima at 252 nm in phosphate buffer 7.4

Calibration curves of Lidocaine :

Standard graphs of Lidocaine were plotted in different mediums i.e. phosphate buffer pH 7.4, phosphate buffer pH 7.4 containing phosphate buffer pH 7.4. The standard graph of Lidocaine in phosphate buffer pH 7.4 showed good correlation between concentration and absorbance with R^2 value of 0.997.

Table 2: Standard graph of Lidocaine in phosphate buffer 7.4

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0
1	0.124
2	0.227
3	0.342
4	0.449
5	0.530

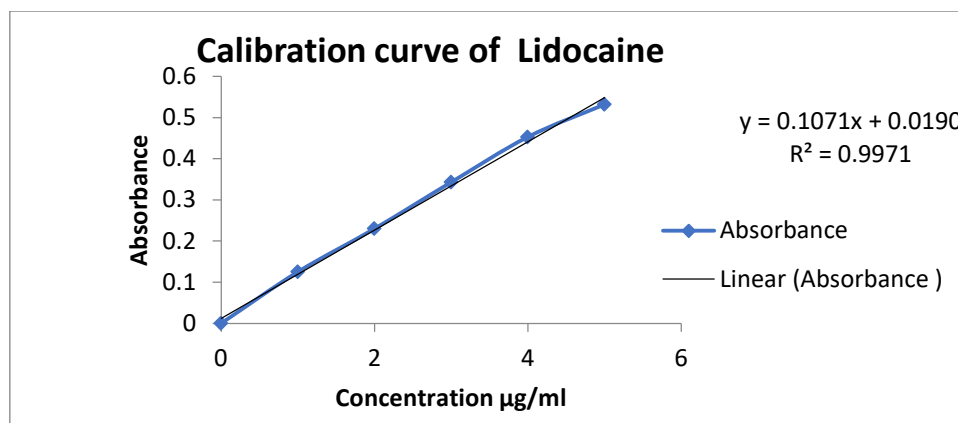


Fig 1: Standard graph of Lidocaine in phosphate buffer 7.4

FT-IR Spectrum of Lidocaine

FT-IR Spectra of Lidocaine and polymers were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Lidocaine and polymers. It also confirmed that the stability of drug during process.

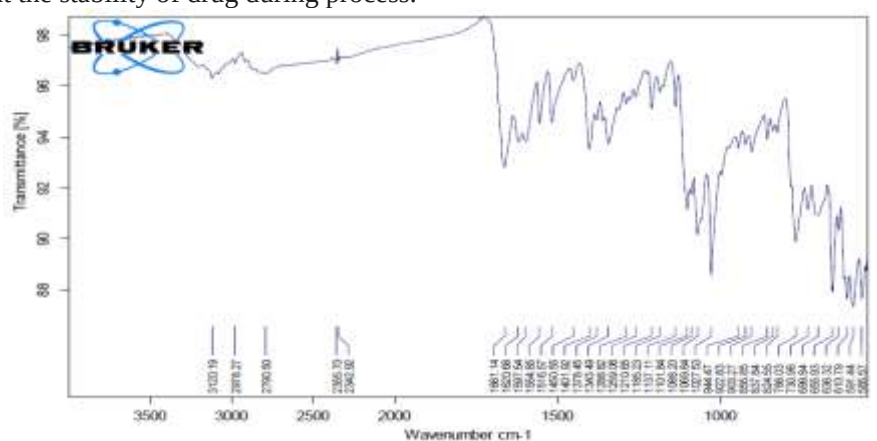


Fig 2: FT-IR Sample for Lidocaine

Table 3: Characteristic Peaks and frequency of Lidocaine

S. No.	Characteristic Peaks	Frequency range (cm^{-1})	Frequency (cm^{-1})
1	OH stretching	3500-3000	3120.19
2	OH Bending	3000-2500	2790.50
3	C-H stretching	2000-1500	1661.14
4	C-N stretching	1500-1000	1027.53

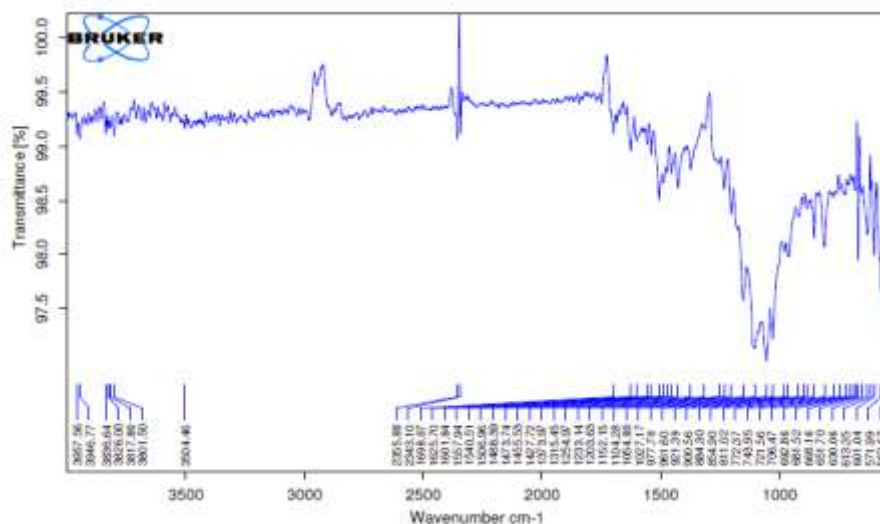


Fig 3: FT-IR Sample for physical mixture of drug and Excipients

Table 4: Characteristic Peaks and frequency of physical mixture of drug and Excipients

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3000	3504.46
2	OH Bending	3000-2500	2355.88
3	C-H stretching	2000-1500	1233.14
4	C-N stretching	1500-1000	1027.17

Evaluation of Transdermal formulation

Table 5: Physicochemical evaluation of Lidocaine patches

Formulation code	Weight (mg)	Thickness (mm)	Folding endurance	Drug content (%)	% Moisture loss	% Moisture absorption
F1	153	0.38	163	82.59	7.3	9.5
F2	149	0.42	172	80.42	7.5	9.7
F3	153	0.45	182	79.53	7.2	9.3
F4	165	0.49	183	82.46	7.9	9.8
F5	159	0.50	179	83.26	8.1	9.5
F6	162	0.52	182	90.25	8.3	9.8
F7	168	0.56	168	85.63	7.8	9.8
F8	163	0.58	180	93.56	8.9	10.1

Discussion

The physicochemical evaluation of the prepared lidocaine transdermal patches demonstrated satisfactory characteristics with respect to weight variation, thickness, folding endurance, drug content, moisture loss, and moisture absorption. These parameters are important indicators of the quality, uniformity, mechanical strength, and stability of transdermal patches.

The weight of the prepared formulations ranged from 149 mg (F2) to 168 mg (F7). The slight variation in weight among the formulations may be attributed to differences in polymer concentration and the amount of casting solution used during film preparation. However, all formulations exhibited

acceptable weight uniformity, indicating consistent casting and uniform distribution of the formulation components.

The thickness of the patches varied between 0.38 mm (F1) and 0.58 mm (F8). An increase in film thickness was observed with increasing polymer concentration, particularly in formulations containing higher amounts of sodium alginate. Thicker films are expected due to the greater quantity of polymer present, and the uniform thickness obtained across all formulations ensures consistent drug loading and controlled drug release.

The folding endurance values ranged from 163 (F1) to 183 (F4), indicating excellent flexibility and mechanical strength of the prepared films. Formulations F4 and F3/F6 exhibited the highest folding endurance values (183 and 182, respectively), suggesting that the polymeric films were sufficiently elastic to withstand repeated folding without cracking. The incorporation of PEG as a plasticizer contributed significantly to improving the flexibility of the patches.

The drug content ranged from 79.53% (F3) to 93.56% (F8). The higher drug content observed in formulations containing increased concentrations of sodium alginate suggests improved drug entrapment and more uniform dispersion of lidocaine within the polymeric matrix. Formulation F8 exhibited the highest drug content (93.56%), followed by F6 (90.25%), indicating efficient incorporation of the drug during the solvent casting process. The results demonstrate satisfactory drug content uniformity across all formulations.

The percentage moisture loss was found to range between 7.2% (F3) and 8.9% (F8). Lower moisture loss values indicate better moisture retention within the polymeric matrix, which helps maintain flexibility and prevents brittleness during storage. Although formulations containing higher polymer concentrations showed slightly higher moisture loss, the observed values remained within acceptable limits and did not adversely affect the integrity of the films.

The percentage moisture absorption ranged from 9.3% (F3) to 10.1% (F8). The slightly higher moisture absorption exhibited by formulations containing greater amounts of sodium alginate is attributed to the hydrophilic nature of the polymer, which readily absorbs atmospheric moisture. Nevertheless, the moisture absorption values were acceptable and indicated good stability of the prepared patches under normal environmental conditions.

***In vitro* release study:**

Table 6: *In vitro* drug release profiles of Lidocaine transdermal patch (F1-F8)

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	17.36	18.12	16.97	17.86	13.69	14.69	18.59	19.72
2	28.13	27.46	25.84	28.61	27.46	25.66	26.37	28.10
3	36.91	35.20	36.78	38.48	35.48	30.19	32.56	33.50
4	56.68	52.34	45.80	47.82	46.33	42.13	46.98	48.79
6	64.92	65.50	65.92	69.86	67.82	62.33	63.58	65.81
8	75.15	76.34	77.89	79.81	72.15	70.18	73.25	75.81
10	84.62	85.19	80.12	86.52	81.25	82.35	86.35	89.83
12	93.64	95.46	93.26	98.88	92.36	94.69	97.82	98.35

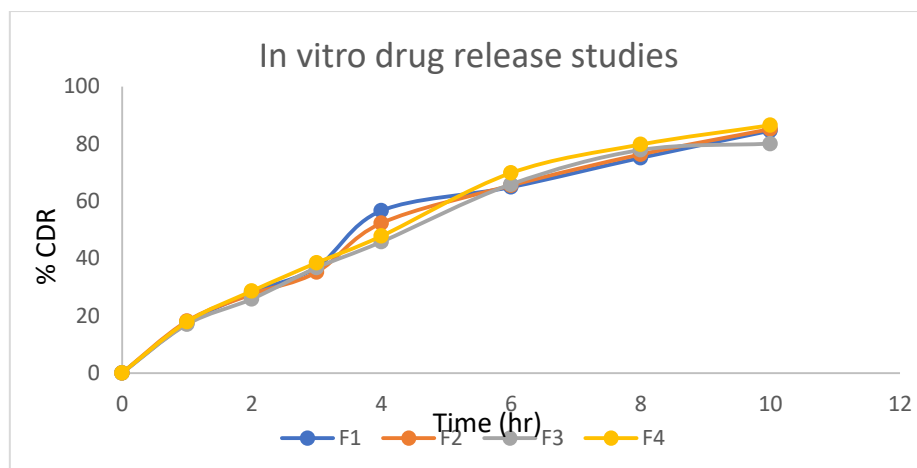


Fig 4: Drug release for (F1-F4) formulations

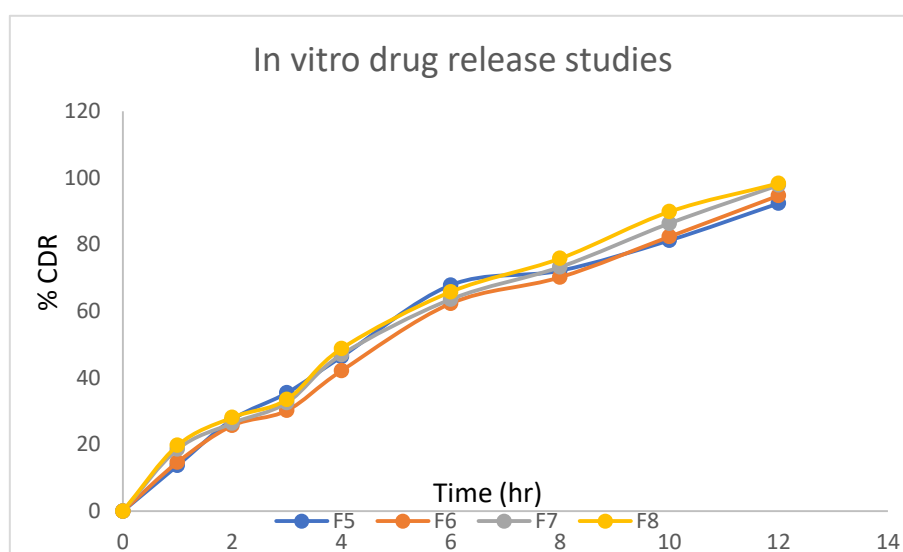


Fig 5: Drug release for (F5-F8) formulation

Discussion

Overall, the prepared polymeric transdermal patches successfully provided sustained drug release over 12 hours, demonstrating the suitability of the solvent casting method for the development of controlled-release transdermal systems. Among all formulations, F4 was identified as the optimized formulation because it combined the highest cumulative drug release (98.88%) with satisfactory physicochemical characteristics. These findings indicate that F4 has excellent potential for sustained transdermal delivery of lidocaine, ensuring prolonged therapeutic action, reduced dosing frequency, and improved patient compliance.

Kinetic models:

Table 7: Drug Release Kinetics of Formulation F8

Time (hrs)	%CDR	SQARE T	LOG T	LOG%CDR	ARA	LOG%ARA
0	0	0	0	0	100	0
1	19.72	1	0	1.294906911	80.28	0
2	28.1	1.41421	0.29103	1.44870632	71.9	0.15051
3	33.5	1.73205	0.45712	1.525044807	66.5	0.23856

4	48.79	2	0.62689	1.688330818	51.21	0.30103
6	65.81	2.44949	0.70815	1.818291891	34.19	0.38908
8	75.81	2.82843	0.91031	1.879726497	24.19	0.45154
10	89.83	3.16228	0.96025	1.9534214	10.17	0.5
12	98.35	3.4641	1.07449	1.992774364	1.65	0.53959

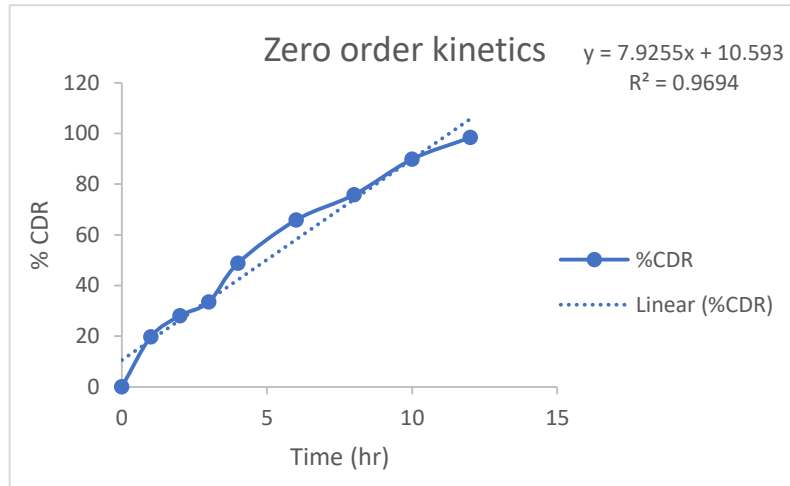


Fig 6: Zero order kinetics of optimized formulation

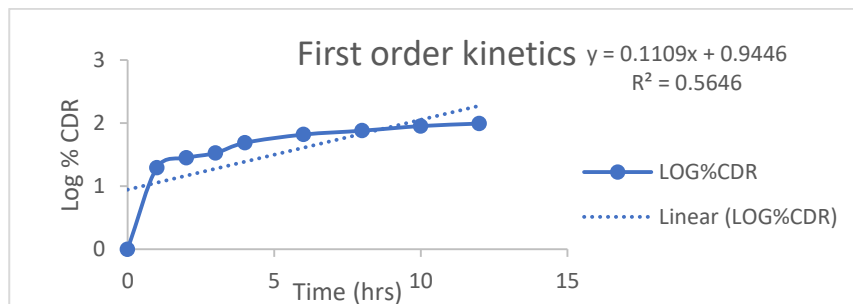


Fig 7: First order kinetics of optimized formulation

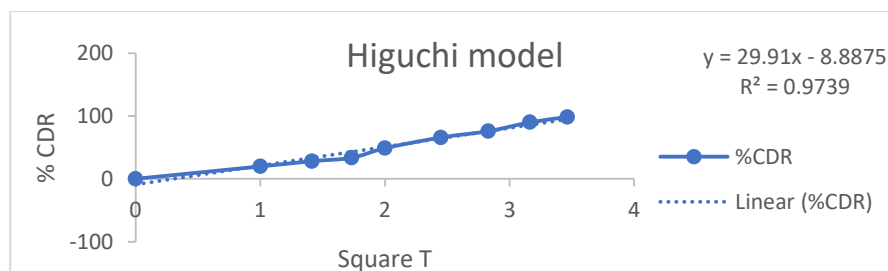


Fig 8: Higuchi model of optimized formulation

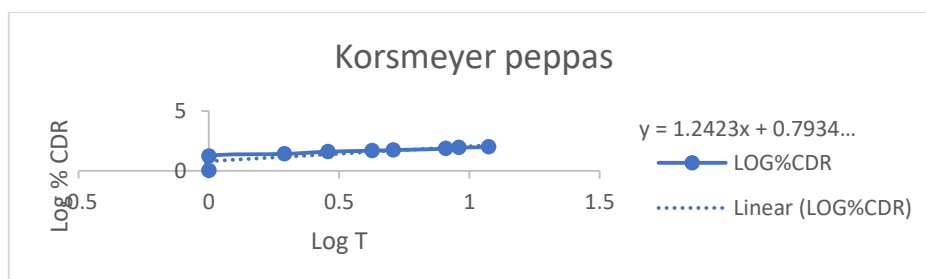


Fig 9: Korsmeyer peppas of optimized formulation**Table 8: Regression equations of optimized formulation**

F. No	In vitro release in phosphate buffer P ^H 7.4 Regression values			
	Zero order	First order	Higuchi Plot	Korsmeyerpeppas
F8	0.969	0.564	0.973	0.669

Discussion

Overall, the kinetic analysis demonstrated that the optimized formulation F8 exhibited diffusion-controlled sustained drug release, with the Higuchi model providing the best fit ($R^2 = 0.973$), followed closely by the Zero-order model ($R^2 = 0.969$). These results indicate that the sodium alginate-based polymeric matrix effectively regulated the release of lidocaine over 12 hours, making formulation F8 a promising sustained-release transdermal drug delivery system capable of providing prolonged therapeutic action and improved patient compliance.

STABILITY STUDIES

Table 9: Stability studies of optimized formulations at 40 ± 2 °C and $75 \pm 5\%$ RH for 3 months

Time in days	Drug content (%)	Folding endurance	Physical appearance	% Cumulative drug release
0	93.56	180	No change in color	98.35
90	92.50	178	Slight yellowish color	97.82

Discussion

Overall, the accelerated stability study demonstrated that the optimized formulation F8 possessed excellent physical, mechanical, and chemical stability over the 90-day storage period. The negligible changes in drug content, folding endurance, physical appearance, and cumulative drug release indicate that the formulation remained stable and retained its sustained-release characteristics under accelerated conditions. These findings confirm that the optimized lidocaine polymeric transdermal patch has good storage stability, making it a suitable candidate for long-term pharmaceutical use and further clinical development.

CONCLUSION

The present investigation successfully demonstrated the development and characterization of polymeric transdermal patches of lidocaine for sustained drug delivery using the solvent casting technique. The prepared formulations exhibited satisfactory physicochemical properties, good mechanical strength, adequate flexibility, and acceptable moisture characteristics, indicating their suitability for transdermal application. Among the developed formulations, F8, containing 400 mg of sodium alginate, emerged as the optimized formulation based on its highest drug content (93.56%), excellent mechanical properties, sustained drug release (98.35% at 12 hours), and good stability during accelerated storage. Drug release kinetic analysis indicated that the release mechanism predominantly followed the Higuchi diffusion model, confirming diffusion-controlled sustained drug release from the polymeric matrix. The stability studies further established that the optimized formulation retained its physical integrity, drug content, and release characteristics throughout the storage period, demonstrating good shelf stability. The incorporation of PEG and D-limonene further enhanced the flexibility of the patches and facilitated efficient drug permeation. Overall, the developed lidocaine polymeric transdermal patch represents a promising sustained-release drug delivery system capable of providing prolonged therapeutic action, reducing dosing frequency, minimizing systemic side effects, and improving patient compliance. The optimized formulation has significant potential for the management of pain and may serve as an effective alternative to conventional oral or injectable dosage forms. Further ex vivo skin permeation studies, in vivo pharmacokinetic evaluations, and clinical investigations are recommended to establish its therapeutic efficacy and commercial applicability.

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