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Development and Characterization of Self-healing Transdermal Patch of Lidocaine for the Management of Pain

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ABSTRACT

Pain management is a significant challenge due to the side effects associated with commonly prescribed medications like NSAIDs and opioids. Local anesthetics, such as lidocaine, offer an alternative with fewer side effects when formulated in topical patches. Transdermal delivery systems, including heated patches, enhance drug absorption and provide targeted pain relief. This research paper aims to develop and characterize a self-heating transdermal patch of lidocaine for pain management. The drug sample of lidocaine was characterized using UV-visible spectrophotometric analysis, melting point determination, and differential scanning calorimetry. The results confirmed the purity of the drug sample. Pre-formulation studies were conducted to determine the solubility and partition coefficient of lidocaine, as well as drug-excipient interaction studies. The formulation of the lidocaine transdermal patch included the selection of excipients such as solvents, adhesives, solubilizers, and permeation enhancers. The patch was developed in three trial batches, with the final batch prepared using a drug-in-adhesive type approach. The developed patch was evaluated for physical characteristics, solvent residual content, rolling ball test, shear strength, drug crystallization, drug content, and in-vitro permeation. The results of the evaluation showed that the developed lidocaine transdermal patch had the desired physical characteristics, uniform thickness, good folding endurance, and appropriate solvent residual content. It exhibited satisfactory rolling ball test and shear strength. Microscopic examination confirmed the absence of drug crystallization. The drug content of the patch was determined to be within the desired range, and the in-vitro permeation study demonstrated successful drug release through the dialysis membrane. In conclusion, the development and characterization of a self-heating transdermal patch of lidocaine for pain management provide a promising approach for effective and targeted pain relief. The patch formulation demonstrated suitable physical properties, drug content, and permeation characteristics, suggesting its potential as an alternative pain management solution.

Key words: Lidocaine, transdermal patch, pain management, self-heating, drug delivery.

1. INTRODUCTION

Pain, the unwelcome companion of disease, manifests as a distressing sensory and emotional experience linked to actual or potential tissue damage.[1] It comes in two forms: acute, which is short-lived and often follows surgery or trauma, and chronic, which persists long after healing should have occurred.[2] Whether caused by arthritis, cancer treatments, fibromyalgia, or past injuries, pain demands a solution.[3] While medications like NSAIDs and opioids are commonly prescribed, their notorious side effects cannot be overlooked. From headaches and drowsiness to gastrointestinal problems and physical dependence, these drawbacks hinder the quest for optimal pain management.[4]

However, a new ray of hope emerges through the realm of local anesthetics. Offering distinct advantages over conventional analgesics, they effectively numb the affected area without the dizzying side effects associated with opioids. When formulated in a topical manner, these agents open up a vast landscape for the development of pain-relief solutions.

By bypassing the drawbacks of oral medications, topical formulations provide instant relief while increasing patient compliance.[4,5]

One notable example is the lidocaine patch, delivering targeted peripheral analgesia without relying on complex delivery systems. By "dampening" pain mechanisms in the peripheral nervous system, these patches offer localized pain relief with remarkable precision. In contrast, transdermal delivery systems, like transdermal fentanyl, boast a slower onset and extended duration of analgesia, typically spanning 12 to 18 hours.[6]

Heat therapy is a game-changer in pain management, offering profound benefits for relaxation, tissue healing, and targeted relief. It effectively soothes painful muscles, chronic discomfort, and joint pain. By increasing circulation and blood flow, even a slight rise in temperature brings relief and enhances muscle flexibility. Heat transforms transdermal medication delivery by augmenting skin permeability, fluid circulation, and drug solubility. It boosts the kinetic energy of drug molecules, widens skin penetration channels, and improves absorption. Studies confirm that heated patches significantly elevate lidocaine levels in the bloodstream, enhancing drug distribution and optimizing absorption. Heat therapy unlocks a new era of pain relief and personalized drug administration, empowering individuals to regain control over their well-being. Let us embrace the power of heat, revolutionizing pain management and drug delivery for a brighter future.[7,8]

Lidocaine is a local anesthetic that is also used as an adjuvant analgesic to relieve pain. As with opioids, lidocaine has pharmacological activity by numbing the afflicted area without causing disorientation. A transdermal lidocaine formulation allows for the creation of a wide range of effective formulations. It can avoid the negative effects of oral analgesics while providing excellent pain relief and increasing patient compliance. Therefore, the current work aims to prepare and develop a heating lidocaine patch to overcome the lag time of a standard lidocaine patch and boost the drug flux through skin that is depoted in a commercially available transdermal patch.

2. MATERIALS & METHODS

2.1 Sample Material

Drug Sample was purchase from the local medicine market of Gwalior, Madhya Pradesh, India.

2.2 Characterization of Drug Sample

UV-visible spectrophotometric analysis, melting point determination, and differential scanning calorimetry were used to characterize the lidocaine drug sample obtained. The melting point, UV-visible spectroscopy, and DSC findings were compared against standard values. Based on the findings, it was determined that the drug sample obtained was pure and hence employed for future research.

2.2.1 Determination of λmax for Estimation of Lidocaine by UV Spectroscopic Method

A precisely weighed amount of lidocaine (50 mg) was dissolved in 50 ml of phosphate buffer (pH 6.8), and the volume was then increased to 100 ml by phosphate buffer (pH 6.8) to yield a 500 µg/ml solution. The solution's uv spectra were then scanned between 200 and 400 nm on a Shimadzu-1700 double beam uv-visible spectrophotometer, and max was calculated.

2.2.2 Melting Point Determination

The melting point of a lidocaine drug sample was evaluated using the open capillary tube method. The drug sample was placed in a capillary tube attached to a thermometer in a thiele's tube filled with liquid paraffin. The tube was heated, and the temperature at which the drug sample melted was recorded.

2.2.3 Differential Scanning Calorimetry Analysis

DSC-6000 (PerkinElmer Thermal Analysis) was used to analyze a lidocaine medication sample. Two milligrams of lidocaine were inserted and sealed in an aluminium pan, which was subsequently heated from 50 to 150 degrees Celsius at a scanning rate of 10 degrees Celsius per minute under nitrogen flow (20 ml/min). As a guide, an empty aluminium pan was used.

2.3 Pre-formulation Studies

2.3.1 Preparation of Calibration Curve of Lidocaine in Phosphate Buffer (pH 6.8) and Ethanol

Lidocaine (50mg) was diluted in 100 mL of pH 6.8 phosphate buffer and ethanol. The resulting solution was further diluted to obtain concentrations of 100, 200, 300, 400, and 500 µg/ml. UV-visible spectrophotometry at 263 nm (Shimadzu 1700 double beam) was used for measurement.

2.3.2 Determination of Solubility of Lidocaine

The solubility of lidocaine drug sample was evaluated in different solvents: pure water, phosphate buffer saline (pH 7.4 & 6.8), ethanol, oleic acid, ethyl acetate, propylene glycol, and isopropyl alcohol. Excess medication was added to vials containing 1 ml of each solvent, which were then sealed and agitated for 10 minutes using a vortex mixer. The solutions were subsequently filtered using Whatman filter paper no. 41, appropriately diluted,

and analyzed spectrophotometrically at 263 nm using a UV-visible spectrophotometer (Shimadzu 1700®).

2.3.3 Determination of Partition Coefficient

The partition coefficient of lidocaine was determined at 37 °C using a separating funnel with 10 ml octanol and 10 ml phosphate buffer (pH 6.8). A 10 mg dose of lidocaine powder was added to the separating funnel and agitated for 24 hours. The resulting two layers were separated and filtered. The amount of lidocaine dissolved in phosphate buffer (pH 6.8) was measured at 263 nm using a UV-visible spectrophotometer. The amount of lidocaine dissolved in octanol was calculated by subtracting the amount in phosphate buffer (pH 6.8) from the total obtained in the separating funnel. The log P value was then determined.[9]

2.3.4 Drug Excipient Interaction Studies

The physical compatibility of the medication and excipients was assessed by mixing them in a 1:1 ratio. The vials were sealed and stored under different conditions: refrigerated at 2-8 °C, at ambient temperature of 25 °C, and at accelerated temperature of 40 °C. Weekly extractions were performed over a month, and the contents of each vial were examined for changes in physical appearance and color.[10]

2.4 Formulation & Development of Lidocaine Transdermal Delivery Patch

2.4.1 Selection of Excipients

The lidocaine transdermal patch formulation included selected excipients such as solvents, adhesives, solubilizers, and permeation enhancers. The permeation enhancer was chosen based on its ability to improve lidocaine permeation, with a 1:1 eutectic mixture of camphor and menthol showing the highest penetration compared to other options. The solvent with the optimal drying time and solubility for both the drug and excipients was selected. Adhesives and solubilizers were chosen based on their solubility and ability to form a stable matrix.

2.4.2 Formulation of Lidocaine Transdermal Patch

The lidocaine transdermal patch was developed in three trial batches. One batch using Biopsa 4302 adhesive was discontinued due to a failure in transferring the coated matrix to the backing membrane from the release liner. The remaining two batches of the lidocaine transdermal patch were subjected to separate evaluation tests and utilized DuroTak 87-2287 and Durotak 87-6908 adhesives.

2.4.2.1 Procedure for Formulation of Lidocaine Transdermal Patch (trial batch 1)

The insoluble and water-soluble components were weighed and placed in a sealed vial. The soluble components were added to the insoluble component and mixed using a vortex mixer for 10 minutes. The formulation was then left to stand for thirty minutes. Subsequently, the formulation was filled into its packaging, and the temperature of the packaged system was monitored. The target GSM (grams per square meter) of the lidocaine transdermal patch was 125 GSM (140 cm).[11]

2.4.2.2 Procedure for Formulation of Lidocaine Transdermal Patch (Trial Batch 2)

A 5% lidocaine drug solution was prepared by dissolving the measured amount of lidocaine in a mixture of solvent (n-heptane), permeation enhancer (camphor and menthol), and medium-chain triglyceride. The medication solution was added slowly to pre-weighed adhesive while stirring continuously. The adhesive-containing medication solution was then poured onto a release liner after stirring. The coated release liner was dried in an oven at 55°C for one hour and subsequently laminated with a backing membrane to facilitate coating transfer. The target GSM (grams per square meter) of the formulated lidocaine transdermal patch was 125 GSM (140 cm).[12]

2.4.2.3 Formulation of Final Batch

In the present study, drug-in-adhesive type lidocaine transdermal patch was prepared.

2.5 Evaluation of Developed Lidocaine Transdermal Patch Formulation

2.5.1 Physical Evaluation of Developed Lidocaine Transdermal Patch Formulation

The physical evaluation of the fabricated transdermal patch was performed by using electronic digital micrometer (Mitutoyo-China) for thickness, digital weighing machine for uniformity of weight and manually folded for folding endurance.[13]

2.5.1.1 Thickness Uniformity

The thickness of drug containing adhesive matrix was determined by measuring the thickness of whole patch using 5 different point and subtracting the thickness of the backing membrane and release liner. The average was determined by using electronic digital micrometer (Mitutoyo-China) for thickness.[14]

2.5.1.2 Folding Endurance and Weight Variation

A strip of specific area (2*2 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film was folded at the same place without breaking gave the value of the folding endurance.[15]

2.5.2 Solvent Residual Content of Developed Lidocaine Transdermal Patch Formulation

This test was performed to determine how much solvent remained in the formulated transdermal patch. The individually prepared transdermal patch was baked for 12 hours at 50°C before being weighed on a digital weighing machine. The residual solvent was estimated using weighed difference.

2.5.3 Rolling Ball Test of Developed Lidocaine Transdermal Patch Formulation

The distance travelled by a stainless steel along the upward face of adhesive is measured in this test. The ball had a diameter of 7/16 inch and was released on an inclined track with an inclination of 22.50°. The adhesive becomes less tacky as it travels further. The amount of adhesive was calculated by measuring the distance travelled by the ball in inches.[16]

2.5.4 Shear Strength of Developed Lidocaine Transdermal Patch Formulation

The patch was cut into strips 2 cm broad and 8 cm long. The liner was removed from one end and patch was applied on the stainless-steel plate such that 5 cm long strip was stuck on to the stainless-steel plate with a 3 cm attaching length. The opposite end was secured with hooks, and 500 gm was applied to the hook. The time necessary for the patch to fall was measured.[17]

2.5.5 Drug Crystallization Study of Developed Lidocaine Transdermal Patch Formulation

A polarizing microscope (Leica) with a magnification of 100X and an oil immersion lens was used to study drug crystallization. A drug solution containing adhesive, permeation enhancer, and solubilizer was applied to a glass slide and dried before being examined under a microscope for crystal formation.

2.5.6 Drug Content of Developed Lidocaine Transdermal Patch Formulation

A piece of the formed patch was cut and placed in 100 ml of phosphate buffer (pH 7.4) solution, which was magnetically agitated for 2 hours. The solution was then filtered through Whatman filter paper (0.45) and the drug content was determined using a Shimadzu 1700 double beam uv/visible spectrophotometer at 263 nm.[18]

2.5.7 In vitro Permeation Study of Developed Lidocaine Transdermal Patch Formulation

Dialysis membrane treatment (Hi Media 70) For one hour, the cellophane membrane was cooked in distilled water. It was then cleaned three times with fresh distilled water and stored in alcohol for one day. It was rinsed again, treated with 0.3% sodium sulfite, and then steeped in distilled water for 2 minutes at 60° C, followed by acidification with 0.2% sulfuric acid. After washing with distilled water, the membrane was washed with phosphate buffer (pH 7.4) and utilized for drug permeation tests.[19]

2.5.8 Permeation Through Franz Diffusion Cell

At 330.5° C, in vitro permeation was done using a dialysis membrane (HiMedia 70) gran diffusion cell in phosphate buffer (pH 7.4). It had a compartment and a receptor compartment. A small magnetic bead is then spun at a steady speed of 100-200 rpm through the receptor solution. The dialysis machine was installed between the donor and www.compartment. The drug releasing surface was put to the dialysis membrane after the release liner was removed from a cut piece of patch 4*4. The receptor compartment of the cell was filled with phosphate buffer (pH 7.4). The assembled item was placed on the magnetic stirrer. The temperature was 32 +0.5C. The diffusion fluid was withdrawn at various time intervals and drug levels were determined by Shimadzu 1700 double beam UV- visible spectrophotometer at 263 mm.[20]

3. RESULTS AND DISCUSSIONS

3.1 Drug Characterization

3.1.1 Physical Characteristics

The lidocaine sample obtained was crystalline and white in colour. Water was essentially insoluble, whereas organic solvents were soluble.

3.1.2 Determination of λ max for Estimation of Lidocaine by UV Spectroscopic Method

The lidocaine UV spectra showed a peak at 263 nm, which confirmed the drug lidocaine.

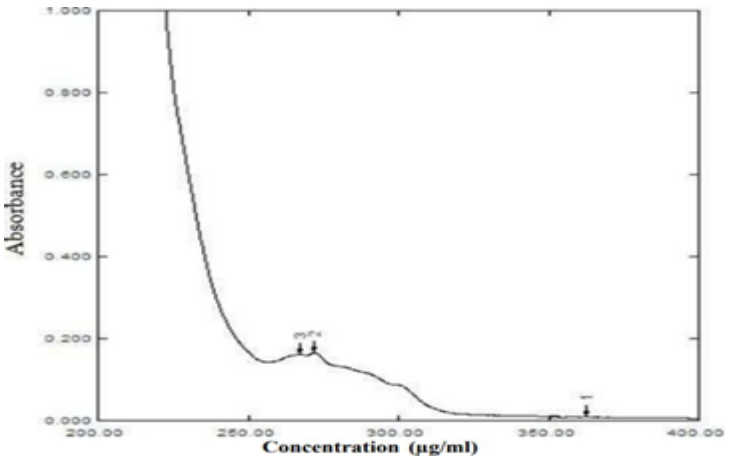

Figure 1: UV spectrum of lidocaine in phosphate buffer (pH 6.8)

3.1.3 Melting Point Determination

The melting point of lidocaine drug sample was found within the range of 68- 70º C.

3.1.4 Differential Scanning Calorimetry Analysis

The lidocaine differential scanning thermogram revealed that it melts at 69°C, which was identical to the value reported in the literature.

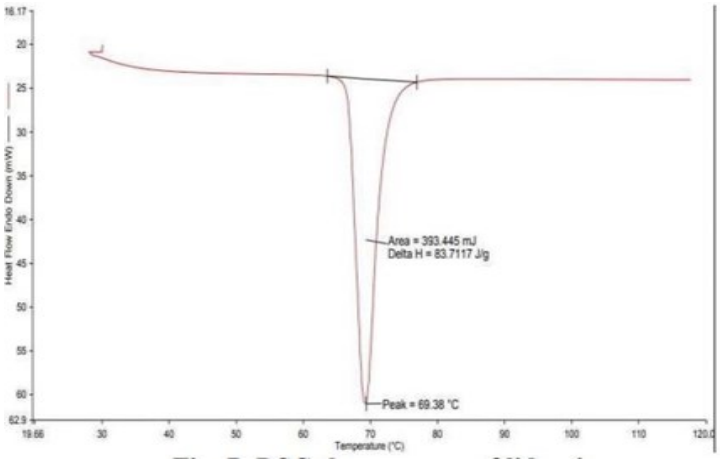

Figure 2: DSC thermogram of lidocaine

Melting point determination, uv-visible spectroscopy, and differential scanning calorimetry were used to characterize the lidocaine sample obtained. The analysis results were found to be comparable to the values reported in the literature for the reference lidocaine sample. This confirmed that the drug sample obtained was pure lidocaine, which was then used for further research.

3.2 Pre-formulation Studies

3.2.1 Preparation of Calibration Curve of Lidocaine in Phosphate Buffer (Ph 6.8)

Table 1: Absorbance data of lidocaine dilutions in phosphate buffer (pH 6.8) at 263 nm.

S. No.	Drug concentration (µg/ml)	Absorbance	
		Phosphate buffer (Ph 6.8)	Ethanol
0	0	0	0
1	100	0.196	0.138
2	200	0.377	0.287
3	300	0.565	0.448
4	400	0.744	0.587
5	500	0.944	0.765

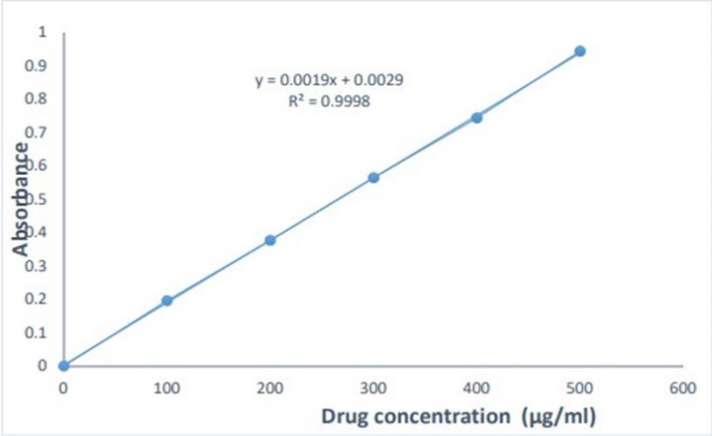

Figure 3: Calibration curve of lidocaine in phosphate buffer (pH 6.8) at 263 nm.

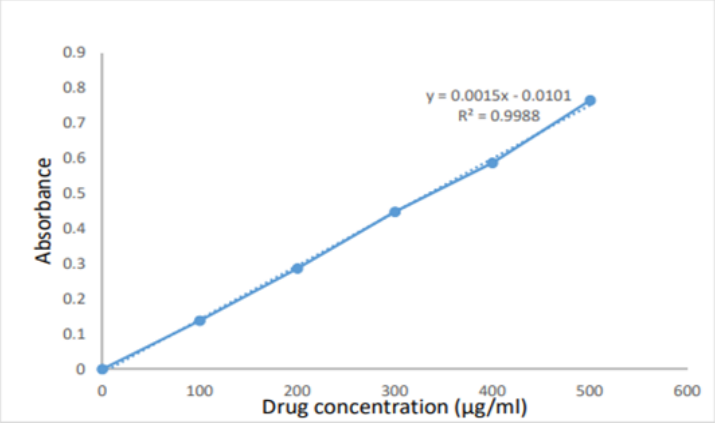

Figure 4: Calibration curve of lidocaine in phosphate buffer (pH 6.8) at 263 nm.

3.2.2 Determination of Solubility of Lidocaine

Table 2: Solubility of lidocaine in different solvent media

S. No.	Solvent media	Solubility
1.	Purified water	Very slightly insoluble
2.	PBS (pH 7.4)	Very slightly soluble
3.	PBS (pH 6.8)	Very slightly soluble
4.	Ethanol	Very soluble
5.	Oleic acid	Freely soluble
6.	Ethyl acetate	Very soluble
7.	Propylene glycol	Freely soluble
8.	Isopropyl alcohol	Very soluble
9.	n-heptane	Very soluble
10.	Eutectic mixture of (camphor & menthol)	Soluble

3.2.3 Determination of Partition Coefficient

The partition coefficient of lidocaine was found to be 2.44, which showed that the drug is lipophilic in nature.

3.2.4 Drug Excipient Interaction Studies

Table 3: Drug-Excipient interaction studies

S. No.	Drug-Excipient blend	Ratio	Observation of initial appearance	Observation at different time intervals		
				Refrigerated temperature2-8°C, Room Temperature 25°C, & Accelerated temperature 40°C		
				Duration (weeks)		
				1.	2.	3.
1.	Lidocaine	1:1	White crystalline powder	N	N	N
2.	Lidocaine + Durotak 87-2287	1:1	Transparent mass	N	N	N
3.	Lidocaine + Durotak 87-6908	1:1	Transparent mass	N	N	N
4.	Lidocaine + Biopsa 4302	1:1	Transparent mass	N	N	N
5.	Lidocaine + Camphor	1:1	White mass	N	N	N
6.	Lidocaine + Menthol	1:1	Clear solution	N	N	N
7.	Lidocaine + Solubilizer	1:1	Clear solution	N	N	N
8.	Lidocaine + Ethyl acetate	1:1	Clear solution	N	N	N
9.	Lidocaine + n-Heptane	1:1	Clear solution	N	N	N

A thorough examination revealed no evidence of drug-excipient interaction. The medication and excipient were determined to be stable at refrigerated, accelerated, and room temperatures.

3.3 Formulation & Development of Lidocaine Transdermal Delivery Patch

3.3.1 Selection of Excipients

Duratak 87-2287 adhesive was selected for its compatibility with the drug and other components, including the release liner and backing membrane. Ethyl acetate was chosen as a solvent to reduce the high viscosity of Duratak 87-2287 adhesive during patch fabrication. The amount of iron in the formulation was found to affect the duration of heat production, with a higher iron content resulting in longer heat generation. The presence of carbon and a suitable concentration of xanthan gum contributed to heat retention, while vermiculite improved the overall heat

retention property. Water content influenced the maximum temperature (Tmax) and excessive water slowed down the thermogenic characteristics of the patch. Medium chain triglyceride was selected as a solubilizer and penetration enhancer, preventing drug crystallization in the patch. Camphor and menthol (1:1) were chosen as the permeation enhancer based on their superior penetration profile. Adhesives Duratak 87-2287, Duratak 87-6908, and Biopsa 4302 were selected for their safety, sticking nature, viscosity, and solubility characteristics.

Table 4: Final composition of self-heating system

S.No.	Components	%w/w
1.	Iron	50%
2.	Carbon	15%
3.	Vermiculite	8.6%
4.	Xanthan gum	0.4%
5.	Potassium chloride	4%
6.	Water	22%

3.3.2 Formulation of Lidocaine Transdermal Patch Patch Formulation (Final Batch -1)

In the present study, drug-in-adhesive type lidocaine transdermal patch was prepared.

Table 5: Formulation composition of lidocaine transdermal patch

S.no	components	%w/w	Weight (gm)
1.	Lidocaine	5%	0.056 gm
2.	Silica	5%	0.056 gm
3.	Medium chain triglyceride	10%	0.112 gm
4.	Dura-tak 87-2287	80%	0.900 gm
5.	Ethyl acetate	-	-
Heat generating system			
1.	Iron	50%	10 gm
2.	Activated charcoal	15%	3 gm
3.	Vermiculite	8.6%	1.72 gm
4.	Xanthan gum	0.4%	0.08 gm
5.	Potassium chloride	4%	0.8 gm
6.	water	22%	4.4 gm

The Self-heating transdermal patch of lidocaine final batch was formulated successfully and further evaluation studies were performed.

3.4 Evaluation of Developed Lidocaine Transdermal Patch Formulation

3.4.1 Physical Evaluation of Developed Lidocaine Transdermal Patch Formulation

3.4.1.1 Thickness Uniformity

Table 6: Thickness of transdermal patch

S. No.	Sample	Thickness
1.	Release liner	0.08
2.	Backing membrane	0.19
3.	Total patch	0.61± 0.03
4.	Matrix	0.34±0.03

3.4.2 Solvent Residual Content of Developed Lidocaine Transdermal Patch Formulation

Table 7: Percent residual solvent of developed lidocaine transdermal patch formulation

S. No.	Formulation	% Residual content	Average
1.	Patch 1	0.12%	0.12%
2.	Patch 2	0.15%	
3.	Patch 3	0.1%	

3.4.3 Rolling Ball Test of Developed Lidocaine Transdermal Patch Formulation

Table 8: Distance travelled by ball through Final batch I and II

S. No.	Distance travelled by ball	
	Final batch – I	Final batch – II
1.	1.2 inches ± 0.1	1.4 inches ± 0.1

3.4.4 Shear Strength of Developed Lidocaine Transdermal Patch Formulation

Table 9: Shear strength of developed lidocaine transdermal patch formulation

S. No.	Time required by	
	Final batch - I	**Final batch – II**
1.	6 min.	4 min. 30 seconds

3.4.5 Drug Crystallization Study of Developed Lidocaine Transdermal Patch Formulation

Table 10: Crystal growth in weeks of developed lidocaine transdermal patch formulation

Final batch	**Crystal growth in weeks**		
Matrix blend of final batch	1	2	3
	No	No	No

3.4.6 Drug Content of Developed Lidocaine Transdermal Patch Formulation

Table 11: % residual content of developed lidocaine transdermal patch formulation

S. No.	Formulation	% Residual content
1.	Patch 1	94.56%
2.	Patch 2	93.11%
3.	Patch 3	92.77%

3.4.7 In-vitro Permeation Study of Developed Lidocaine Transdermal Patch Formulation

Table 12: Drug release profile of developed plain lidocaine patch

S.no	Time (hr)	Cumulative amount of drug permeated (mg/sqcm)	Cpp%	Flux (mg/cm^2 /hr)	Permeability coefficient (cm/hr)
1.	0.5	0.056	7.57	0.0447	0.0223
2.	1	0.156	21.2		
3.	2	0.312	41.63		
4.	4	0.496	66.21		
5.	6	0.566	75.55		
6.	8	0.579	77.32		
7.	10	0.582	77.69		

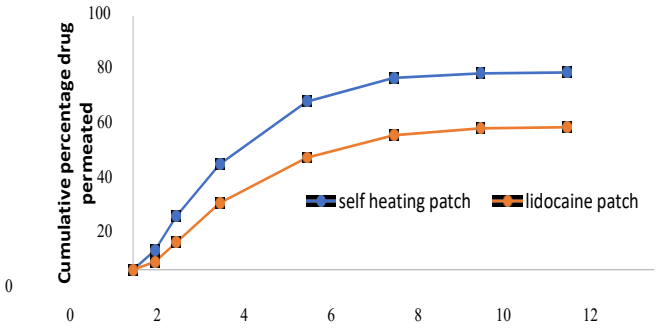

Figure 5: Cumulative percentage drug permeation of developed plain lidocaine patch vs self-heating lidocaine patch

Table 13: Drug release study of developed self-heating topical lidocaine patch

S.No	Time (hr)	Cumulative amount of drug permeated (mg/sqcm)	Cpp%	Flux (mg/cm^2/ hr)	Permeability coefficient (cm/hr)
1.	0.5	0.022	3.01	0.0276	0.0138
2.	1	0.081	10.81		
3.	2	0.197	26.26		
4.	4	0.330	44.10		
5.	6	0.397	52.96		
6.	8	0.417	55.64		
7.	10	0.420	56.07		

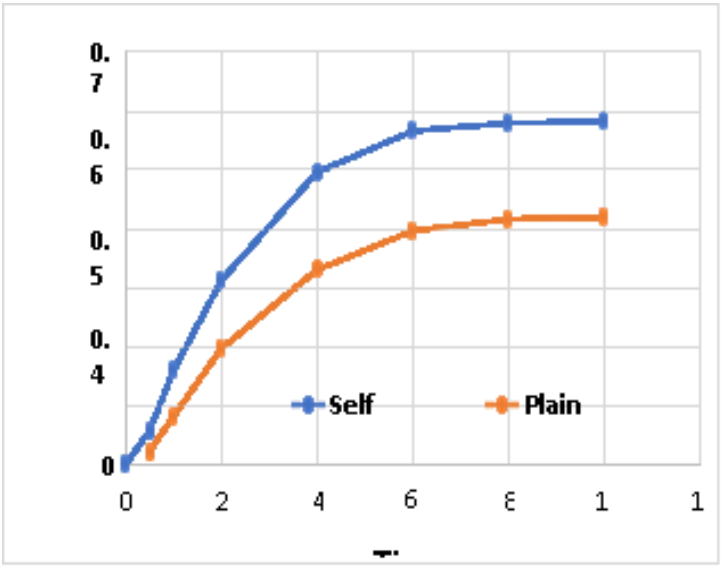

Figure 6: Cumulative amount of drug permeated (mg/sqcm) from developed plain lidocaine-patch vs self-heating lidocaine patch

Table 14: Permeability profile of final batch of transdermal patch

S. No.	ime in hr.	Cumulative amount of drug permeated (mg/sqcm)	CPR (%)	Flux (mg/cm2/hr)	Permeability coefficient (cm/hr)
1.	0	0	0	0.04875	0.02498
2.	1	0.022770013	3.86780573		
3.	2	0.048984667	7.83445012		
4.	3	0.077745664	12.4368232		
5.	4	0.105673446	16.9469903		
6.	5	0.162487981	25.9429169		
7.	6	0.266846723	42.3037731		
8.	7	0.345985467	56.9864709		

3.4.8 Permeation Through Franz Diffusion Cell

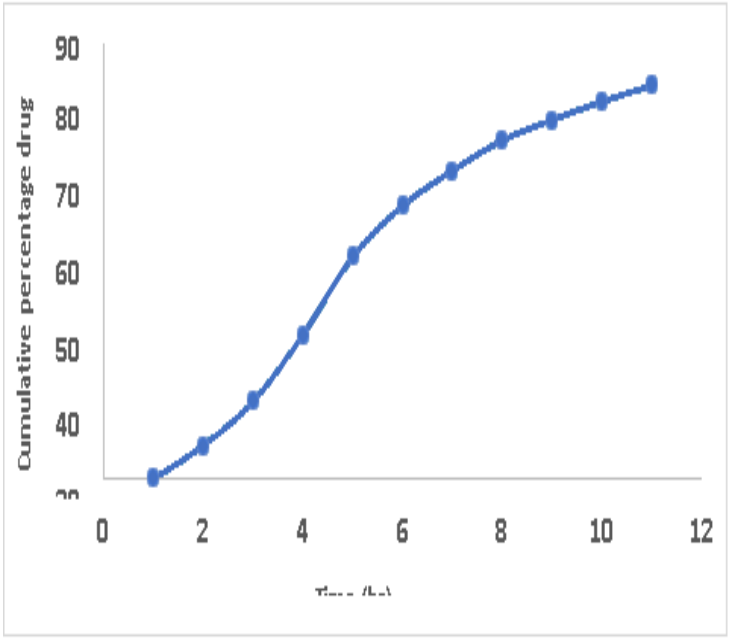

Figure 7: In-vitro drug release of lidocaine transdermal patch formulation

4. CONCLUSION

The development and characterization of a self-heating transdermal patch of lidocaine for pain management provide a promising approach for effective and targeted pain relief. The formulated patch demonstrated suitable physical properties, drug content, and permeation, characteristics, suggesting its potential as an alternative pain management solution. The research showcased the purity of the lidocaine drug sample and conducted pre-formulation studies to determine solubility, partition coefficient, and drug-excipient interactions. The patch formulation included the selection of appropriate excipients, and three trial batches were developed, with the final batch prepared using a drug-in-adhesive approach. The developed patch exhibited desired physical characteristics, uniform thickness, good folding endurance, and satisfactory rolling ball test and shear strength. Microscopic examination confirmed the absence of drug crystallization, and the in-vitro permeation study demonstrated successful drug release through the dialysis membrane. Overall, the self-heating transdermal patch of lidocaine holds promise for effective pain management with improved drug delivery and fewer side effects compared to traditional medications.

REFERENCES

1. Kumar KH, Elavarasi PJJoAC, Insights R. Definition of pain and classification of pain disorders. 2016;3(3):87-90.
2. Finnerup NBJNEJoM. Nonnarcotic methods of pain management. 2019;380(25):2440-8.
3. Świeboda P, Filip R, Prystupa A, Drozd MJP. Assessment of pain: types, mechanism and treatment. 2013;2(7).
4. Verma NK, Panda P, Mishra J, Vishwakarma D, Singh A, Alam GJIJAPIJAP. Advances and development in transdermal drug delivery system—A Review. 2017; 6:49-62.
5. Chien YWJDd, pharmacy i. Development of transdermal drug delivery systems. 1987;13(4-5):589-651.
6. Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LFJEJoP, Biopharmaceutics. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. 2006; 64(1):1-8.
7. Gaikwad AKJCJoPS. Transdermal drug delivery system: Formulation aspects and evaluation. 2013; 1(1):1-10.
8. Jhawat VC, Saini V, Kamboj S, Maggon NJIJPSRR. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. 2013; 20 (1):47-56.
9. Sankar V, Johnson DB, Sivan V, Ravich V, Raghuraman S, Velrajan G, et al. Design and evaluation of nifedipine transdermal patches. 2003;65(5):510.
10. Arora P, Mukherjee BJJops. Design, development, physicochemical, and in vitro and in vivo evaluation of transdermal patches containing diclofenac diethylammonium salt. 2002;91(9):2076-89.
11. Cilurzo F, Gennari CG, Minghetti PJEoodd. Adhesive properties: a critical issue in transdermal patch development. 2012; 9(1):33-45.
12. Pastore MN, Kalia YN, Horstmann M, Roberts MSJBjop. Transdermal patches: history, development and pharmacology. 2015; 172(9):2179-209.
13. Patel RP, Patel G, Patel H, Baria AJRJoPDF, Technology. Formulation and evaluation of transdermal patch of aceclofenac. 2009;1(2):108-15.
14. Prajapati ST, Patel CG, Patel CNJISRN. Formulation and evaluation of transdermal patch of repaglinide. 2011;2011.
15. George TP, Ziedonis DM, Feingold A, Pepper WT, Satterburg CA, Winkel J, et al. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. 2000; 157(11):1835-42.
16. Dhiman S, Singh TG, Rehni AKJIJPPS. Transdermal patches: a recent approach to new drug delivery system. 2011; 3(5):26-34.
17. Ren C, Fang L, Ling L, Wang Q, Liu S, Zhao L, et al. Design and in vivo evaluation of an indapamide transdermal patch. 2009; 370(1-2):129-35.
18. Ah Y-C, Choi J-K, Choi Y-K, Ki H-M, Bae J-HJIJoP. A novel transdermal patch incorporating meloxicam: in vitro and in vivo characterization. 2010; 385(1-2):12-9.
19. Gannu R, Vamshi Vishnu Y, Kishan V, Madhusudan Rao YJCDD. Development of nitrendipine transdermal patches: in vitro and ex vivo characterization. 2007; 4(1):69-76.
20. Al Hanbali OA, Khan HMS, Sarfraz M, Arafat M, Ijaz S, Hameed AJAP. Transdermal patches: Design and current approaches to painless drug delivery. 2019; 69(2):197-215.