wjpmr, 2023, 9(12), 109-119

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

DEVELOPMENT AND EVALUATION OF LABETALOL HCL MATRIX TRANSDERMAL PATCHES FOR THE TREATMENT OF HYPERTENSION

***Bhatia Anirudh (Research Scholar) and Khalid Mohammed**

Krishna Pharmacy College, Bijnor, Uttar Pradesh.

***Corresponding Author: Bhatia Anirudh**

Research Scholar, Krishna Pharmacy College, Bijnor, Uttar Pradesh.

Article Received on 13/09/2023 **Article Revised on 02/11/2023** **Article Accepted on 23/11/2023**

ABSTRACT

Labetalol HCl is an antihypertensive medication used to treat hypertension. Its oral bioavailability is only 25% due to first-pass metabolism, and it has a half-life of 6 hours. Given the 100mg maximum daily dose, frequent dosing was required. To enhance bioavailability and improve patient compliance, Labetalol HCl transdermal patches were developed. Different formulations were created by adjusting the proportions of HPMC, Methyl Cellulose, and PVP using the solvent casting method. These formulations were evaluated for various factors, including weight variation, patch thickness, folding durability, drug content, moisture absorption and loss rates, and in-vitro drug release. A chemical compatibility study of Labetalol HCl with the polymers was conducted using FTIR Spectrometry, confirming that there was no interaction between the drug and polymers. Standard graphs were created for Labetalol HCl, demonstrating linearity (R2=0.998) and adherence to Beer's and Lambert's law. Through a 32 complete factorial design, the impact of changing the proportions of HPMC (X1) and PVC (X2) on the tensile strength and the percentage of medication released in 20 hours (Q20) were determined. Regression analysis and analysis of variance were performed on the dependent variables. It was concluded that Labetalol HCl could indeed be formulated into transdermal patches for controlled release. The formulation HPMC, Methyl Cellulose, & PVP (2:1) F4 was identified as the most suitable for controlled release, releasing 96.20% of the medication in 24 hours. The goal of this research was to administer the medication through intact skin at a controlled rate to increase bioavailability and extend the duration of hypertension treatment using transdermal patches. The skin offers numerous advantages over other routes of drug administration, such as avoiding issues related to gastric irritation, gastric emptying rate, hepatic first-pass metabolism, and minimizing the risk of systemic side effects.

KEYWORDS: Hypertension, Labetalol HCl, Enhance Bioavailability, Transdermal Patches, Controlled Release.

INTRODUCTION

Transdermal Drug Delivery System

The oral and perenteral routes are the most common routes of drug delivery with the majority of small molecule drug traditionally delivered orally. The oral route has the advantage of predetermined doses and self-administration. For this basis, the oral route remains the most convenient means of delivering medication. But, most therapeutic peptides and proteins are not delivered by the oral route. Logically, the conventional routes of medication have many limitation which could likely be overcome by advanced drug delivery methodologies such as transdermal drug delivery. Transdermal delivery represents an attractive alternative to oral delivery of drug; low bioavailability is most accepted problem for the oral dosage form of water soluble drugs. TDDS has a verity of advantages compared with oral route. It is a painless method of delivering drugs systemically by applying a drug formulation onto the healthy skin.[1-4]

Ideal Drug Candidates Suitable for TDDS

- Low molecular weight (less approx 500 Daltons).
- Low melting point (less than approx.200 degree C).
- Dose is ideally less than approx 10-50 mg per day is recommended.
- Should be non-ionic.

Advantages of TDDS

- Avoid first pass GI and hepatic metabolism.
- Greater patient compliancy due to an elimination of multiple dosing.
- More uniform plasma levels.
- Enhance therapeutic efficiency.
- Non-invasive & painless.
- Improved bioavailability.
- Continuous sustain release.

MATERIALS AND METHODS

Procurement of Drug & Chemicals

Labetalol HCl was collected as a gift sample from Care Formulation Labs Pvt.ltd. Narela, New Delhi, India and it was analyzed visually for physical appearance. Methocel, Methyl Cellulose, Dimethyl Sulfoxide, Dimethyl Formamide, Tewwn-80, Polythylene Glycol, Dibutyl Pthalate, Chloroform, Methonol, etc was received as a gift sample from Finecure Pharmaceuticals Ltd, Malsa Road, Shimala Pistore, Uddham Singh Nagar & Uttarakhand, India.

Pre-formulation Studies

Physical Appearance of Drug

Labetalol HCl was collected as a gift sample from Finecure Pharmaceuticals Ltd, Malsa Road, Shimala Pistore, Uttarakhand, India and it was analyzed visually for physical appearance. It was usually defined on the basis of organoleptic properties such as colour, odour and taste. All these physical domains were compared with announced in official study (Indian Pharmacopoeia, 2007).

Identification of Drug

Melting Point

The drugs melting point's was obtained by using a capillary fusion technique. A capillary tube was taken it nearby the burner flame, and then sealed at one side. The open side of the capillary tube was pushed into a little number of drugs, or the tube was tapped softly. This procedure was copied a lot of times. Then the capillary tube was kept in the melting point assurance apparatus or noticed the temp. At which sample modify its state from solid to liquid. The examination was achieved in triplicate. The temp. At which starts to melt was notable with help of the thermometer and it was correlated with the previous reported value [Prajapati ST et. al., 2011].

Identification of Labetalol HCl by Visible Spectrophotometrically Methods

10 mg of drug (Labetalol HCl) was dissolved in 10ml of Potassium hydrogen phthalate pH 7.4 buffer and diluted with methanol up to 100ml. 1ml sample of the solution was diluted up to 10 ml with 10% v/v Potassium hydrogen phthalate 7.4 buffer. After the dilution the solution was investigated in the UV spectrophotometer b/w 200/400nm. The UV spectra of the drug was taped and compared with reported abs. max [Prajapati ST et. al., 2011].

Scanning of Labetalol HCl in Different Solvent Method

10mg of Labetalol HCl was dissolved in 100ml of other solvents such as water, methanol, and Potassium hydrogen phthalate 7.4 buffer or a solution of 100µg/ml were prepared as a stock solution. From this solution of 0.5ml, 1ml, 2ml, 3ml, 4ml, 5ml, 6ml, 7ml, 8ml, 9ml, 10ml was taken or the volume was made up to 10ml with equal solvents. These solutions to make solution conc. 5µg/ml, 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml, 60µg/ml, 70µg/ml, 80µg/ml, 90µg/ml, 100µg/ml. The final solution was scanned by using UV-visible spectrophotometer. The observation was fulfilled in ternary manner & abs. max were noted [Shalu rani et al, 2011].

Preparation of Curve of Labetalol HCl

10mg Labetalol HCl was dissolved in 50 ml of appropriate solvent (i.e. water, methanol, and Potassium hydrogen phthalate 7.4 buffers) and the solvent was mixed regularly beside a clear solution formed. The clear solution was mainly classified up to 100 ml with same solvent. 1 ml of this solution carries 100µg of Labetalol HCl. Again 1 ml of this solution was mainly mixed up to 10 ml with respective solvent system to form 10µg/ml solution. Now 1ml, 2ml, 3ml, 4ml, 5ml, 6ml, 7ml, 8ml, 9ml, 10ml of mixed solution were taken and mainly diluted to 10ml with respective solvent solution. After the dilution the solution were determined diluted solutions was examine using a UV spectrophotometer at greatest them every experiment was carried out in triplicate form and a concentration Vs abs. was scheme for preparation of calibration curve and R2 were regulate.[5-6]

Solubility Study

Solubility of the drug was proved, because solubility of drug is directly proportional to the drug free from the formulation commonly drug absorbed into the blood stream. The solubility of drug was studied in the dissimilar solvents like water, ethanol, H2O, Dimethyl Formamide, DMSO, Benzyl Alcohol & Phenol. Standard buffers solutions were develop as per the procedure given in IP 2007. The solubility of Labetalol HCl was set by adding excess amount of drug in flask with respective solvent system and kept under agitated and black conditions at 25 degree Celsius in h2o bath shaker for 24 hours & examine after 24 hours [Rao VJ et. al., 2010].

Partition Co-efficient of Labetalol HCl

The partition coefficient is a measure of lipophilicity of a molecule, which can be used to calculate its capability to cross biological membrane. The oil water partition coefficient is mainly conceded and by using two immiscible solvents and the almost suitable and mainly solvent like ethanol, methanol, ethyl acetate, and ether & alcohol are in use with water for examining the partition coefficient of molecules or drug deliberate. Mix flask method is most common way to examine partition coefficient [Rao VJ et. al., 2010].

Procedure

The partition coefficient of the Labetalol HCl was executed by taking same volumes of methanol or water solvent system in a separating tube. Exactly weighted 10 mg of drug delivery was taken and mixed it in immiscible solvent system like 25ml distilled water and 25ml methanol. This solution of methanol and distilled water was taken in separating tube and continuous mixed for 10 minutes and permit it to stand for 1 hr**.** After 1 hr

both the surface of solvents were separated, and centrifuged for 10 minutes at 2000rmp. It was examine by UV-spectrophotometer to get the partition coefficient and regulate the amount of drug after suitable dilution. Every sample determines in triplicate from & average value was calculated. Coefficient of drug in layer of methanol and layer of water phase was calculated by using the following partition coefficient formula mention below.[7]

Partition coefficient (K) = Conc. in organic phase / Conc. in aqueous phase.

Drug Excipients Interaction Studies

Drug and excipients interactions compatibility studies were move out on the basis of physical and chemical compatibility data was calculated study. Where as physical compatibility data was calculated in table form and FTIR and DSC studies confirmed the molecular level of interaction of drug with other excipients, which was mention in FTIR spectra and DSC analysis part.[8]

FTIR Study

In the formulation of transdermal patches polymer and drugs may communicate as they are in much near contact with one another, which could show to the instability of drug. Pre-formulation studies concerning the polymers and interactions are consequently very difficult in selecting suitable polymers. FTIR a spectroscopy was employed to ascertain the compatibility b/w Labetalol HCl & the selected polymers. The pure drug, polymers, physical mixture off drug and polymers and formulation were subjected to FTIR studies by FTIR spectrophotometer to monitor the interactions of drug with excipients were move b/w the value of 4000cm-1 to 450 cm-1 wave number. FTIR spectrum of Labetalol HCl was collated with FTIR spectra of Labetalol HCl with polymer. The pure drug and drug with excipients were search separately [kumar D et. al., 2010].

DSC Studies

The thermal analysis of pure Labetalol HCl, PVP, HPMC, transdermal patches (blank or medicated patches), and physical mixture of drug and polymer and fraction were move out b dissimilar scanning calorimetry (DSC) equipped with thermal analysis data system (Mettler Toledo). Sample weighing 1-2mg were heated in flat - bottomed sealed aluminium pans over a temperature range of 30 to 300℃ at a constant rate of 10℃/min under nitrogen purge (50 ml/min) [kumar D et. al., 2010].

Formulation of Transdermal Patch

Development of Blank Transdermal Film

The formulation of drug free films was developed by solvent casting method employing glycerol as a substrate. The casting solution was developed by mixed appropriate polymers and plasticizers and these were contains in suitable solvents with the help of magnetic stirrer until a homogeneous mixture was formed. The solutions were then poured into the Petridis and permit to dry and to control the solvent evaporation rate an inverted flask over the Petridis was put on it and left for one day without any disturbance at room temperature. The films could do recover intact by slowly lifting from the petriplates and packed in the desiccators until used [Madhulatha et. a., 2013].

Table 1: Formulation of Labetalol HCl Patches.

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Labetalol HCl	100	100	100	100	100	100
Methocel	200	200	200	200	200	200
Methyl Cellulose	2	4	6	2	4	6
Dimethyl Sulfoxide	2	4	6	2	4	6
Dimethyl Formamide	0.1	0.2	0.3	0.4	0.5	0.6
Polyethylene Glycol	3	6	9	3	6	9
Dibutyl Pthalate	1	2	3	1	2	3
Methanol	10	10	10	10	10	10
Chloroform	0.2	0.3	0.4	0.2	0.3	0.4
Tween-80	0.4	0.4	0.4	0.4	0.4	0.4

Experimental Design

A 3^2 full factorial design was used in the present study. In this design 2 independent factors were assessed each at 3 levels & experimental trials were executed for all possible combinations. The 2 independent formulation variables analysed during the study were proportion of HPMC (X1), and PVP. The selected factors with the actual & coded levels as per the design are show in table. The higher, lower and the intermediate levels of each factor are coded as +1, -1 & 0 respective drug release (y1), total 50% drug release in hr (y2) and folding endurance of patches (y3) [Kumar S et.al., 2010].

Design of Formulations Variables and Development of Medicated Patches

The medicated patches were arranged by solvent casting technique employing glycerol as a substrate. The casting solution were arrange by mixed proper polymers, drug, plasticizers and permeation enhancer were include in fit solvent according to factorial plan and solution was mixed using magnetic stirrer till to get the clear homogeneous combination. The solution was then poured into the Petridis and permit drying and solvent evaporation was maintained by placing an invert funnel over the Petridis. These were left at room temperature for

single day. The patches could be recovered entire by slowly lifting from the Petridis and packed in aluminum foil or kept in the freezer till used.[9-10]

Evaluation of Transdermal Patches

Weight Variation

These patches from each batch were correctly weighed by using a digital weighed by using a digital weighing balance. The average weight and the standard deviation values were calculated from the individual weight [Raju R et. al., 2010].

Thickness of the Patches

The thickness of the transdermal films was measured at three different points using a screw gauge and the average thickness values were calculated for each formulation [Raju R et. al., 2010].

Folding Endurance

Folding endurance was measured to examine the capacity of the films withstands to rupture. Folding endurance of patches was examined by folding a small strip of the film. (2cm x 2cm) continues at the same place without breaking and it's calculated as the folding endurance value of the film [Raju R et. al., 2010].

Drug Content

A particular film was (1cm x 1cm) was break and mixed in enough amount of phosphate buffer saline. The volume was made up to 10ml and 1ml with a withdrawn from this solution and further diluted to 10ml after adding suitable reagent and dilution the solution was filtered by whitman's filter membrane, and the absorbance of the solution was found out at 412nm by using UV-vis spectrophotometer. From the abs. & dilution part. The drug content in the film was calculated. Average drug content of 3 transdermal films was examined [Yogesh M et. al., 2010].

% Moisture Absorption

The film were weighted correctly and placed in the desiccators containing 100ml of saturated solution of aluminium chloried. The individual films were weighed frequently and the patches were taken out, after 3 days or until a fixed weight of film was attain. The percentage of moisture uptake was calculated as the difference b/w final and initial weight with respect to initial weight [Yogesh M et. al., 2010].

% of Moisture Absorption = Final weight - Initial weight / Initial weight x 100.

% Moisture Loss

The patches were weight correctly are kept in a desiccators contain activated silica. The individual files were weighed frequently and the patches were taken out, after 3 days or until a fixed weight of film was attain. The percentage of moisture loss was calculated at the difference b/w initial weight and final weight [Yogesh M et. al., 2010].

Percentage of Moisture Loss = Initial weight - Final weight / Initial weight x 100.

In-vitro Drug Release Study

In-vitro drug release studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 25ml. The cellophane membrane was used for the determination of drug release from the prepared transdermal matrix type patches. The semi-permeable cellophane membrane was mounted b/w the donor & receptor compartment of diffusion cell. The prepared transdermal patch was placed on the cellophane membrane. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4 containing 30% PEG. The whole assembly was fixed on a hot plate magnetic stirrer & solution in receptor compartment was constantly and continuously stirred using magnetic beads & temperature was maintained at 32 ±0.5°C, because the normal skin temperature of human is 32°C. The samples were withdrawn at predetermined time up to 24 hrs & analyzed for drug content at wavelength of 412nm using a Shimadzu UV-1700 double-beam spectrophotometer (Shimadzu, Kyoto, Japan). The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal. Cumulative percentage drug release was calculated using an equation obtained from a calibration curve.[11-12]

Stability Study

The optimized Labetalol HCl Patches formulation F4 kept under accelerated conditions (temperature 40°C±2°C and RH 75±5%) according to ICH guidelines using stability chamber for the period of one month. The samples were withdrawn at 15days predetermined intervals and evaluated for their physical appearance, % Moisture Loss, Folding Endurance & *in vitro* drug release study.[13-15]

RESULTS AND DISCUSSION

Preformulation Study

Physical Appearance of Drug

Table 2: Physical Appearance of Drug.

Parameter	Standard	Result
Colour	White fine Powder	White fine Powder
Odour	**unpleasant**	**unpleasant**
Taste	Bad taste	Bad taste
Melting Point	188°C	187°C

Identification of Labetalol HCl by UV-Spectrophotometrically

Table 3: Calibration data for Analysis of Labetalol HCl in methanol at λ412nm.

S. No.	Conc. (µg/ml)	Abs.
1	0	0
2	5	0.1523
3	20	0.3236
4	30	0.4516
5	40	0.6036
6	50	0.6518
7	60	0.7058
8	70	0.7842
9	80	0.8046
10	90	0.8632
11	100	0.9046

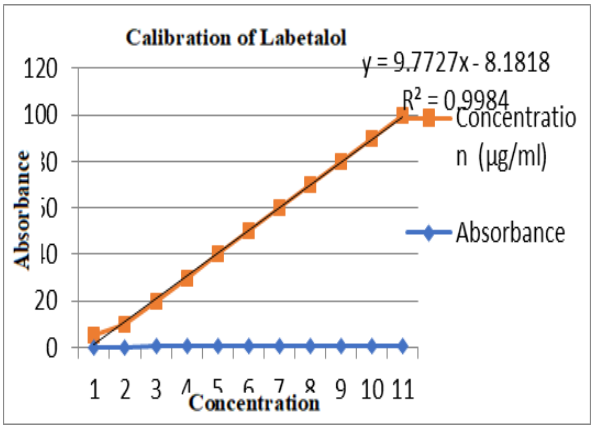

Fig.1: Calibration Curve of Labetalol HCl at 412nm wavelength.

Inference

It was found that the solutions of Labetalol HCl in Potassium hydrogen phthalate 7.4 buffers shows linearity (R2=0.998) in absorbance at concentrations of 05 to 100 mcg/ml and obey Beer Lambert's Law.

Solubility Study

Solubility of Labetalol HCl was checked in various solvents.

Table 4: Determination of drug solubility in various solvents.

S. No.	Solvent	Solubility mg/ml
1	Ethanol	100
2	Water	21.42
3	Liquid paraffin	5.2
4	Glycerine	60.2
5	Propylene glycol	158.20
6	Phenolic	12.98

Process of Determination of Partition Coefficient

Table 3.4: Partition Coefficient.

S.No	Drug (mg)	Methanol (ml)	H2O (ml)
1	100	40	40
2	150	40	40
3	200	40	40

Observation & Calculation of Partition Co-efficient.

Table 5: Calculation of Partition Co-efficient.

S.No.	Conc. of drug in methanol (µg/ml)	Conc. of drug in H2O (µg/ml)	Po/W= Conc. of CH3OH/H2O	Average Po/w
1	0.9135	0.244	5.04	
2	0.720049	0.244	5.02	5.02
3	0. v 9456	0.244	5.12	

FTIR Study

FT-IR spectroscopy gives the possible information about the interaction b/w the drug & polymer. The compatibility between drug & polymer was confirmed by using FT-IR spectroscopy. Infrared spectroscopic analysis for drug (Labetalol HCl), drug polymer admixture and optimized formulations was carried out.

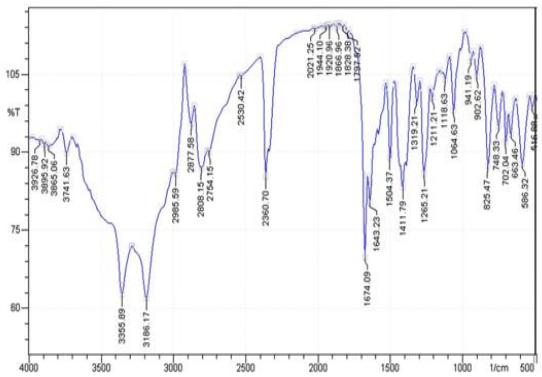

Fig.2: FTIR spectra of Labetalol HCl.

Table 6: FT-IR spectrum interpretation of Labetalol HCl.

Functional group	Characteristic Peaks	Observed Peaks
	Wave number (cm-1)	Wave number (cm-1)
OH Stretching	3200-3700	3445.76
NH Stretching	3000-3400	3236.10
Aromatic-OH	2800-3200	2885.59
Aliphatic CH	2650-2960	2777.58
C=O Stretching	1450-1800	1524
C=C Stretching	1050-1680	1240.13

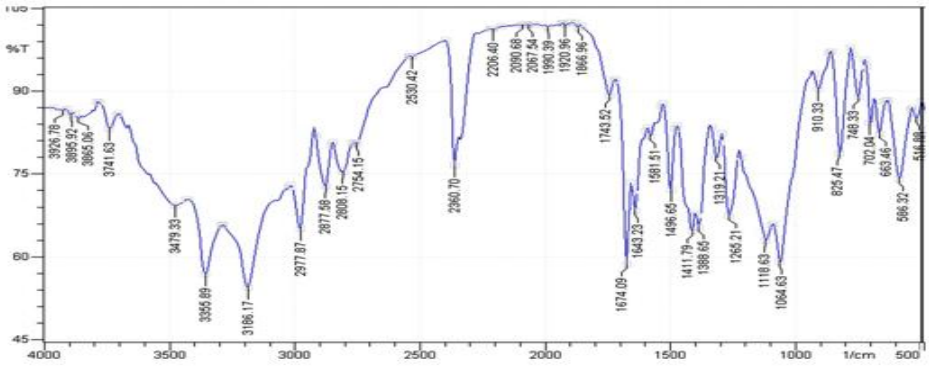

Fig.3: FTIR spectra of Labetalol HCl & HPMC.

Table 7: FT-IR spectrum interpretation of Labetalol HCl & HPMC.

Functional group	Characteristic Peaks	Observed Peaks
	Wave number (cm-1)	Wave number (cm-1)
OH Stretching	3100-3600	3051
NH Stretching	3100-3500	3286
Aromatic-OH	2900-3100	2870
Aliphatic CH	2850-2960	2571
C=O Stretching	1650-1700	1474
C=C Stretching	1620-1680	1248

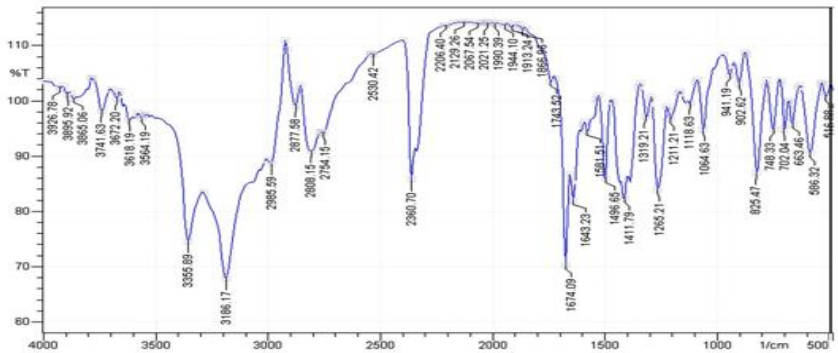

Fig.4: FTIR spectra of Labetalol HCl, Methyl Cellulose & Dimethyl Sulfoxide.

Table 8: FT-IR spectrum interpretation of Labetalol HCl, Methyl Cellulose & Dimethyl Sulfoxide.

Functional group	Characteristic Peaks	Observed Peaks
	Wave number (cm^{-1})	Wave number (cm^{-1})
OH Stretching	3100-3600	3052
NH Stretching	3100-3500	2967.78
Aromatic-OH	2900-3100	2615.76
Aliphatic CH	2850-2960	2427.18
C=O Stretching	1650-1700	1574.08
C=C Stretching	1620-1680	1236.13

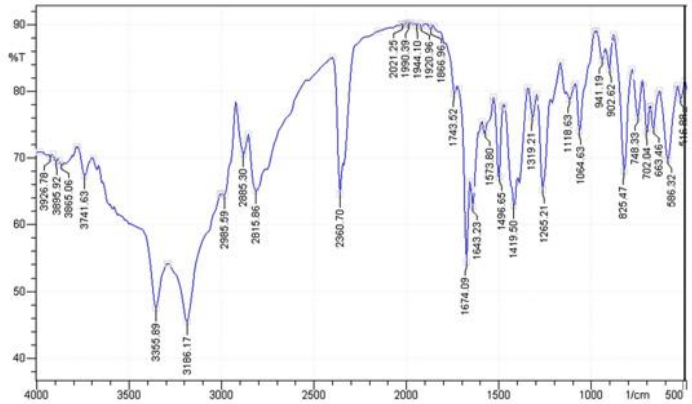

Fig.5: FTIR spectra of Labetalol HCl, Dimethyl Formamide & Tween-80.

Table 9: FT-IR spectrum interpretation of Labetalol HCl, Dimethyl Formamide & Tween-80.

Functional group	Characteristic Peaks	Observed Peaks
	Wave number (cm-1)	Wave number (cm-1)
OH Stretching	3100-3600	3315.19
NH Stretching	3100-3500	3086.18
Aromatic-OH	2900-3100	2915.67
Aliphatic CH	2850-2960	2895.10
C=O Stretching	1650-1700	1678.05
C=C Stretching	1620-1680	1668.13

Inference: There is no disappearance of characteristic peaks of drug in FT-IR Spectra. Hence there is no interaction.

Differential Scanning Calorimetry (DSC) Study

The DSC study was carried out using Mettler Toledo DSC. Samples were placed in an aluminum crucible & DSC thermogram was recorded at heating rate of 100℃/ min in range 30-3000C.

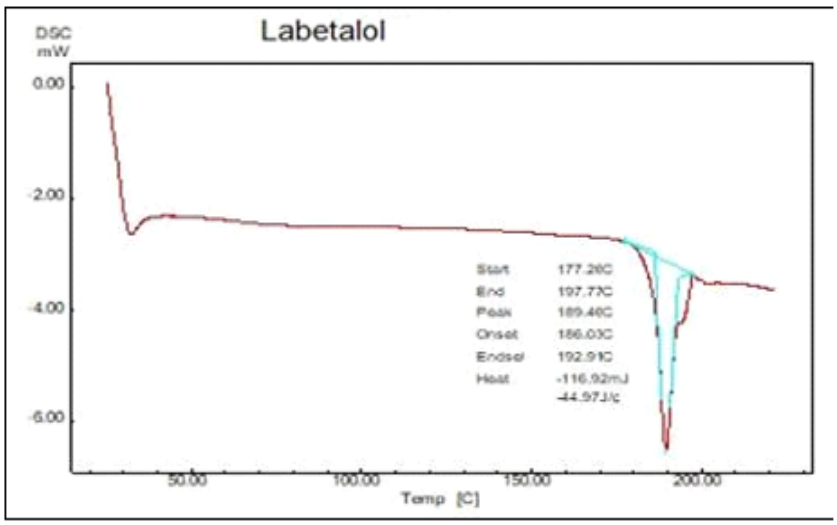

Fig.6: DSC Curve of HPMC - Labetalol HCl.

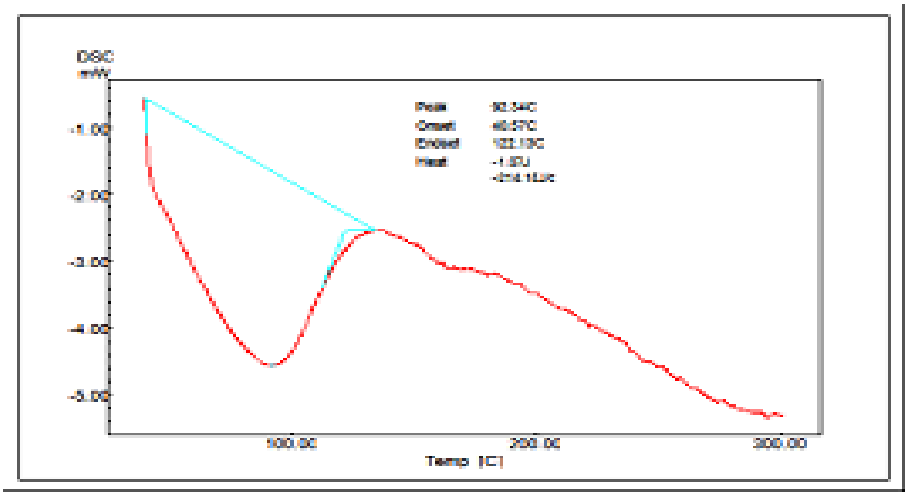

Fig.7: DSC curve of PVP & Labetalol HCl.

Above Figure shows DSC thermo grams of drug, PVP & drug: HPMC (1:2). DSC studies revealed that endothermic peaks for pure Labetalol HCl & HPMC were obtained at 185°C & 187°C respectively. Thermogram of Drug: HPMC complex showed complete disappearance of sharp peak of Labetalol HCl & shift in endothermic peak of HPMC. This indicates successful complexation of Labetalol HCl with HPMC. Thus, DSC studies confirm interaction b/w drug & HPMC.

Experimental Design

Table 10: Design layout for 3^2 Full Factorial Batches.

Batch	Code Value		Actual Value (mg)	
Code	X_1 (HPMC)	X_2 (PVP)	X_1 (HPMC)	X_2 (PVP)
F1	-1	1	100	300
F2	-1	0	100	400
F3	0	1	100	500
F4	-1	-1	200	600
F5	0	0	200	700
F6	0	1	200	700

A statistical model incorporating interactive & polynomial terms was used to evaluate responses: Y=b0 +b1X1 +b2X2 +b12X1X2 +b1 1X1 2+b2 2X2 2, where Y is dependent variable, b0 is the arithmetic mean response of 9 runs & any bi is estimated coefficients for related factor Xi. The main effects (X1 & X2) represent the average result of changing one factor at a time from its low to high value. The interaction term "X1X2" shows how the response changes when two factors change simultaneously. The polynomial terms (X1 2 & X2 2) are included to investigate nonlinearity.

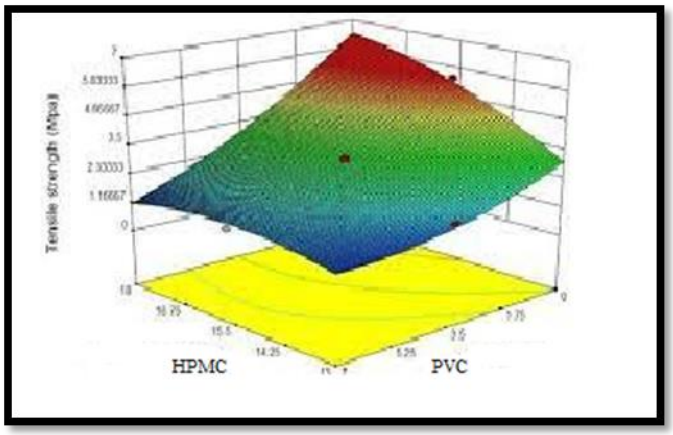

Fig.8: Response surface plot for at 20 hrs.

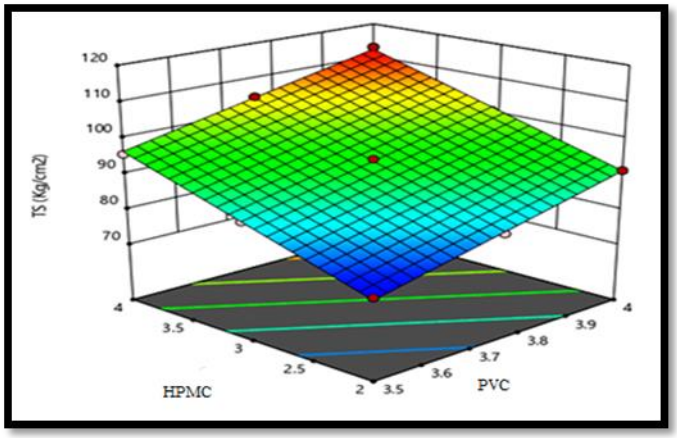

Fig.9: Response surface plot for Tensile Strength.

Evaluation of Transdermal Patches

Physical Appearance of Transdermal Patches

The Labetalol HCl transdermal patches were homogeneous, clear & smooth when prepared. Table.3.8 lists the various patch parameters that have been evaluated.

Table 11: Evaluation of Transdermal Patches.

Batch Code	Weight Variation	Thickness of the Patches	Folding Endurance	Drug Content	% Moisture Absorption	% Moisture Loss
F1	0.250+0.04	0. 24±0.10	58±1	97.14	1.05±0.03	3.10±0.06
F2	0.214+0.01	0.21±0.012	82±4	92.20	1.32±0.06	3.00±0.07
F3	0.230+0.02	0.28±0.004	72±2	96.54	2.01±0.06	2.12±0.08
F4	0.225+0.04	0.32±0.006	68±3	94.34	1.45±0.11	2.98±0.12
F5	0.215+0.05	0.36±0.014	74±4	95.89	1.54±0.04	2.78±0.12
F6	0.298+0.01	0.38±0.016	80±3	93.98	2.00±0.00	2.78±0.04

*Data expressed (±SD); n = 3.

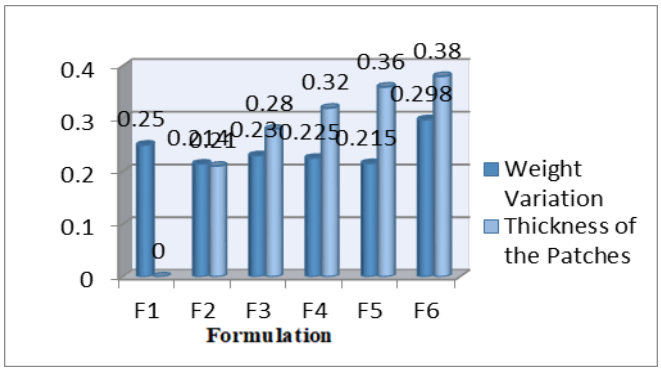

Fig.10: A Representation of Wt. Variation & Thickness.

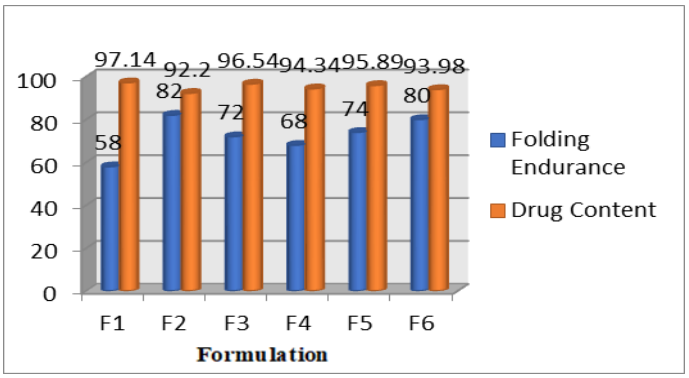

Fig.11: A Representation of Folding Endurance & Drug Content.

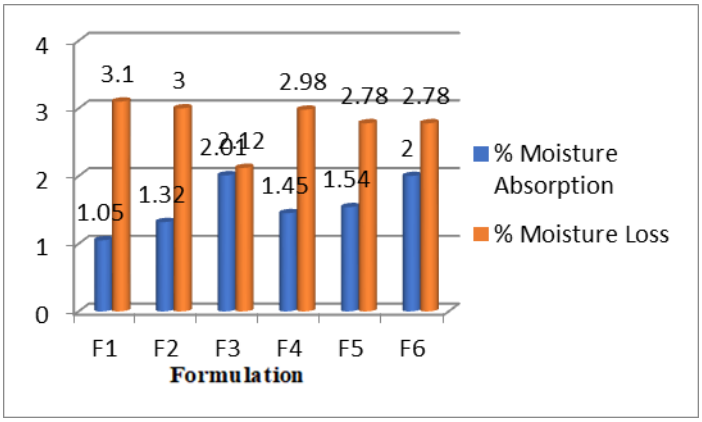

Fig.12: A Representation of % moisture abs. & % moisture loss.

In-Vitro Drug Release Study

Table 12: Cumulative % Durg Release of Formulations F1-F6.

Time Hrs	Cumulative % Durg Release					
Batch No	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
1	10.69	14.75	16.12	18.12	14.02	16.51
2	16.86	28.58	29.12	28.88	20.34	24.44
3	22.93	36.36	37.21	45.46	36.90	38.75
4	38.28	44.58	48.41	56.90	43.90	48.64
6	49.93	52.93	54.65	66.76	52.90	58.51
18	60.99	62.89	66.98	75.34	60.98	68.40
12	69.58	76.65	78.56	85.90	74.90	78.37
24	81.59	88.58	89.12	96.20	86.41	89.26

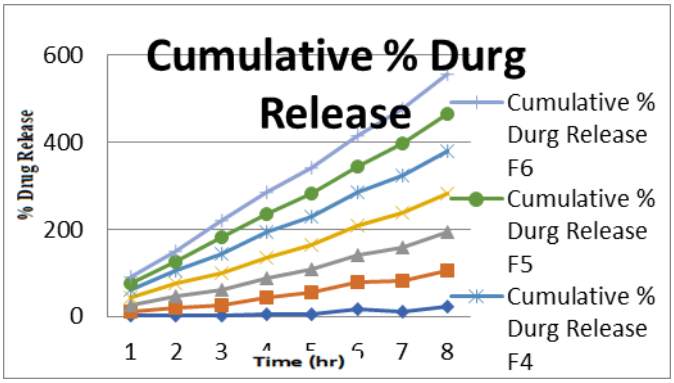

Fig.13: Cumulative % Drug Release of Formulations F1-F6.

Inference

The in vitro drug release profile for formulated Labetalol HCl obtained for F1-F6 formulations were shown in Fig.3.13. Among these the formulations F4 formulation shows (96.20%) controlled release up to 24hrs. Thus, F4 was selected as the optimized formulation.

Stability Studies

Table 13: Stability data for Optimized Formulation F4.

F. code	Stability data for Optimized Formulation F4		
	Zero days	**15days**	**30days**
Physical Appearance	NC	NC	**NC**
% Moisture Loss	2.98±0.12	2.90±0.10	2.68±0.06
Folding Endurance	68±3	67.86±3	67.05±2.5
% Drug Release	96.20	96	95.10

*NC-No change

Inference

The optimized formulations (F4) subjected to stability studies and shown in table.3.13. No significant changes in appearance, Color but small changes in *In-*

vitro drug release, % Moisture Loss & Folding Endurance were observed after the end of 95.10, 2.68±0.06 and 67.05±2.5 for 30 days and found identical in stability studies.

CONCLUSION

A medication used to treat hypertension is called Labetalol HCl. Due to first pass metabolism, it has an oral bioavailability of 25% and a half-life of 6 hours. Since Labetalol HCl has a 100mg daily maximum dose, frequent dosing was necessary. Labetalol HCl transdermal patches were created to increase the drug's bioavailability and patient compliance. By adjusting the proportions of HPMC, Methyl Cellulose, and PVP, different formulations were created using the solvent casting method. The produced formulations were assessed for a number of factors, including weight variation; patch thickness, folding durability, drug content, moisture absorption and loss rates, and in-vitro drug release. Chemical compatibility study of Labetalol HCl with polymers were analysed by using FTIR Spectrometer. The results of the FTIR study proved that there is no interaction between the drug and polymers. Standard graph was drawn for Labetalol HCl and it was found that the solutions show linearity (R2=0.998) and obeyed Beer's and Lambert's law. Using a 3^2 complete factorial design, it was possible to determine how changing the amounts of HPMC (X1) and PVC (X2) would affect the answers, i.e. The dependent variables are the tensile strength and the percentage of medication released in 20 hours (Q20). For dependent variables, regression analysis and analysis of variance were done. It is reasonable to believe that Labetalol HCl can be made into transdermal patches to extend the features of its release. Therefore, it was determined that the formulation HPMC, Methyl Cellulose, & PVP (2:1) F4 was the best for controlled release, releasing 96.20% of the medicine in 24 hours. The goal was to administer the medication over intact skin at a controlled rate to increase bioavailability and extend the duration of hypertension treatment via transdermal patches. The ability to avoid problems with gastric irritation, gastric emptying rate, avoid hepatic first-pass metabolism thereby increasing the bioavailability of drug, and reduce the risk of systemic side effects are just a few of the advantages the skin has over many other routes of drug administration.

REFERENCES

1. Tripathi K. D., 2003. Essentials of Medical Pharmacology. 5th edition. Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, 1–10.
2. Mrs. Aishwarya P Pimple, Miss. Varsha S Kudal, Dr. Gajanan S Sanap, Miss Pooja S Murkute, A Review: Routes of Drug Administration with Their Recent Advances, IJCRT, 2022; 10(2): 421-430.
3. Jean Kim , Orlando De Jesus , Medication Routes of Administration, StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2023.
4. Gaurav Tiwari, Ruchi Tiwari, Birendra Sriwastawa, 2012, Drug Delivery System: An Updated review, IJPI, volume -2, issue -1.
5. Chien Y.W., 2005. Novel Drug Delivery Systems. Marcel Dekker, New York. 2nd edition. volume 1. 1 – 2.
6. Mukesh R Patel, Sustained Released Drug Delivery System: A Patent Overview. volume 1. issue 1, 104. 1-3.
7. Jain N. K., 2004. Controlled and Novel Drug Delivery. CBS Publisher and Distributors, New Delhi. 1st edition. 1 – 2 and 100 – 129.
8. Ahlam Zaid Alkilani, Rayn F Donnelly, Maeliosa. T C McCrudden, Transdermal Drug Delivery: Innovating Pharmaceutical Developments of The Barrier Properties of The Stratum Corneum, 2015; 7(4): 239-240.
9. Kamal Saroha, Bhavna Yadav, Benika Sharma, 2011, Transdermal Patch: A Discrete Dosage Form, Int J Curr Pharm Res, 3(3): 98.
10. Bharat Lal, Manoj Gadewar, 2022, Transdermal Drug Delivery System: A Novel Alternative For Drug Delivery, JPRI, 34(7A): 11.
11. D Prabhakar, J Sreekanth, K N Jayaveera, Transdermal Drug Delivery Patches: A Review, JDDT, 2013; 3(4): 213.
12. Shingade GM, Aamer Quazi, Sabale PM, Review on: Recent Trend on Transdermal Drug Delivery System, JDDT, 2012; 2(1): 67.
13. K.M Siddu; Factors Affecting Transdernal drug Delivery System, 2018; 2-7.
14. Jalwal P., Jangra1 A., Dahiya L., Sangwan Y., Saroha R., 2010. A Review on Transdermal Patches. The Pharma Res, 3: 139-149.
15. Latheeshjlal.L, P. Phanitejaswini, Y.Soujanya, Transdermal Drug Delivery Systems: An Overview, Int.J. Pharm Tech Res, 2011; 3(4): 2143-2144.