RESEARCH PAPER

DESIGN AND DEVELOPMENT OF SUSTAINED RELEASE MATRIX TABLETS OF LABETALOL HCL USING NATURAL AND SYNTHETIC POLYMERS

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ABSTRACT

Labetalol hydrochloride is used in the treatment of hypertension. It has a short half-life and undergoes extensive first-pass metabolism. In the present study, matrix tablets of Labetalol HCl were prepared by direct compression method using Aloe barbadensis, Dioscorea Alata, and Xanthan gum as natural polymers. The purpose of this research was to produce a sustained-release matrix tablet of Labetalol HCl that exhibits higher patient compliance, decreases adverse effects, and enhances oral bioavailability. A sustained-release matrix tablet of Labetalol HCl was manufactured by utilizing a wet granulation process containing 100 mg of Labetalol HCl. The Amount of Aloe barbadensis (X1), Amount of Dioscorea Alata (X2), and Xanthan gum (X3) were chosen as the independent variables. The average weight of tablet formulations was within the range of 348.01–350.40 mg. The measured hardness of tablets of each batch ranged between 6.20–7.40 kg/cm². The percentage drug content of all batches was found between 95.25% to 98.80%. The swelling index increased proportionately with the rate of hydration. Formulations F4–F8 were able to maintain the release of Labetalol HCl for 12 hours. Formulation F8, containing 50 mg of Aloe barbadensis, 20 mg of Dioscorea Alata, and 15 mg of Xanthan gum, was able to swell 90.80% more after 12 hours as compared to other formulations and is therefore considered the optimized formulation. The formulations suggest that the drug transport mechanism follows Fickian diffusion according to the Korsmeyer-Peppas kinetic model. The stability study revealed no significant change in the drug release profile of the F8 formulation.

Keywords: *Labetalol HCl, Aloe barbadensis, Dioscorea Alata, Xanthan gum, FTIR, Sustained Release, Matrix Tablet*

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1. INTRODUCTION

1.1 Oral Drug Delivery

Oral drug delivery has been acknowledged for decades as the most widely applied route of administration among all routes explored for the systemic delivery of drugs through various pharmaceutical products of different dosage forms. The recognition of this route is attributed to its ease of administration and the belief that medications administered orally are well absorbed, analogous to food substances ingested daily.

1.2 Sustained Release Drug Delivery System

In recent years, there has been an increasing effort to develop sustained release dosage forms for many drugs in conjunction with progress and innovation in pharmaceutical technology. The primary objective of this approach is to ensure safety and to improve the efficacy of medicines as well as patient compliance. This is accomplished through better control of plasma drug levels and less frequent dosing. Pharmacokinetic theory indicates that the ideal approach for reducing the plasma maximum concentration (Cmax) to plasma minimum concentration (Cmin) ratio is to achieve zero-order absorption. Once steady state is reached under these conditions, drug concentration in plasma remains constant as long as absorption persists. Successful commercialization of an extended-release formulation is generally complex and involves consideration of many factors including physicochemical properties of the drug, physiological factors, and manufacturing variables.

1.3 Matrix Systems

A matrix tablet is the most effective and cost-efficient technique for fabricating a sustained-release dosage form. The majority of commercially available matrix formulations are in the form of tablets and their manufacture is similar to conventional tablet formulations, including granulation, mixing, compression, and coating steps. In its simplest form, a typical extended-release (ER) matrix system contains a drug, release-retardant polymer (hydrophilic, hydrophobic, or both), one or more excipients (as filler or binder), a glidant, and a lubricant.

1.4 Dissolution of Matrix Systems

The delivery from these systems often follows a time course determined by the choice of polymer and the geometry of the matrix. Such drug delivery systems are suitable for reducing the frequency of drug administration, reducing toxicity for drugs with a narrow therapeutic window, and correcting poor pharmacokinetic behavior such as a short half-life. When solid drug particles are embedded in matrix systems, the release mechanism is more complex than that of solid powder systems and largely depends on the design of the matrix system.

1.4.1 Hydrophilic Matrix System

Cellulosic polymers such as Hydroxypropyl Methylcellulose (HPMC) are mixed-alkyl hydroxyalkyl cellulose ethers containing methoxyl and hydroxypropoxyl groups. The type and distribution of substituent groups affect physicochemical properties such as rate and extent of hydration, surface activity, biodegradation, and mechanical plasticity of the polymer.

1.4.2 Polysaccharides

Natural polysaccharides and their derivatives represent a group of polymers extensively used in pharmaceutical dosage forms. Natural gums have been tested as matrices for the sustained release of drugs. When natural gums in the form of compressed tablets are placed in water, they absorb water from the medium and form a gel before dissolving. If a drug is contained within the tablet, it is released through the gel layer, enabling sustained release. Selected natural polymers and their plant sources are listed in Table 1.

Table 1: Gums and their sources

Natural Gum	Source
Xanthan gum	Xanthomonas campestris
Guar gum	Cyamposis tetragonolobus
Carrageenan	Chondrus crispus and Gigartina stellata
Locust bean gum	Ceratonia siliqua
Scleroglucan	Sclerotium rolfsii
Gellan gum	Pseudomonas clodea

Table 2: Formulation and manufacturing considerations in the design of hydrophilic matrices for sustained release of drugs

Material/Process	Parameters for Considerations
I. Formulation Components	
Drug	Solubility & permeability, pKa, dose, stability, particle size
Polymer	Particle size, type, level
Excipients – Filler	Level/type (solubility)
Lubricants	Level/type (Stearates, non-stearates & fatty acids/oils)
Others	Release rate modifiers, stabilizers, solubilizers, surfactants, buffering agents
II. Manufacturing Aspects	
Direct compression	Particle size of polymer/drug, flow aid
Dry granulation	Slugging/roller compaction
Wet granulation	Aqueous/non-aqueous solvents; water-soluble/insoluble, enteric polymers, fatty acids/waxes

1.5 Relevant Front Description

The matrix contains several fronts: (i) the diffusion front between the gel phase and the glassy or semi-crystalline phase; (ii) the erosion front between the dissolution medium and the eroding surface; and (iii) the swelling front separating dissolved

and undissolved drug within the gel phase. When the system contacts aqueous solution, matrix swelling causes the erosion front to move outward and the swelling front inward. Simultaneously, the diffusion front recedes due to dissolution of solid drug in the gel phase and outward diffusion of dissolved drug. During dissolution, polymer chains at the erosion front disentangle and dissolve, slowing swelling and causing the erosion front to recede at later stages of release.

2. MATERIALS AND METHODS

2.1 List of Materials

The following materials were collected for the experimental work carried out in this study. Details are provided in Tables 3 and 4.

Table 3: List of materials

Sr.	Drug/Excipients	Gifted/Mfg. By
1	Labetalol hydrochloride	Glan Pharma Pvt. Ltd., Hyderabad
2	Captopril	Unicure (India) Pvt. Ltd.
3	HPMC K15M	Sai Mirra Innopharm Pvt. Ltd.
4	HPMC E15	Colorcon Asia Pvt. Ltd.
5	HPMC K4M	Kniss Laboratories
6	MCC	S.D. Fine Chemicals Ltd.
7	Magnesium Stearate	S.D. Fine Chemicals Ltd.
8	Talc	S.D. Fine Chemicals Ltd.
9	Povidone K-30	S.D. Fine Chemicals Ltd.
10	Chitosan	Tristar Formulations Pvt. Ltd.

Table 4: Natural polymer list

Sr.	Polymer	Isolated From	Family
1	Tamarind Gum	Seed	Tamarindus indica (Leguminosae)
2	Tapioca Starch	Root	Manihot esculenta (Euphorbiaceae)
3	Neem Gum	Bark	Azadirachta indica (Meliaceae)
4	Aloe Gum	Leaf	Aloe barbadensis miller (Asphodelaceae)
5	Cassia Roxburghii	Seed	Cassia roxburghii (Caesalpiniaceae)
6	Dioscorea Alata Linn	Tubers	Dioscorea alata Linn (Dioscoreaceae)

2.2 Extraction of Mucilages

2.2.1 Isolation of Tamarind Gum

Collection of seeds → Heating with sand → Coat removal → Hammer milling → Grinding → Sieved using sieve No. 100.

2.2.2 Tapioca Starch Extraction

The wet method described by Ihekoronye and Ngoddy was used for cassava starch isolation. Fresh cassava tuber was manually peeled, washed with clean tap water, and milled into slurries. The slurries were suspended in cold deionized water and sieved to remove fibrous materials, leaving starch in solution. The starch layer was suspended in deionized water and centrifuged 6 to 7 times until the settled starch gave a firm layer.

2.2.3 Extraction of Dioscorea Alata Mucilage

Underground tubers of Dioscorea alata Linn were collected from the Botanical Garden of Noble University in May 2024 and authenticated by Noble Ayurved and Research Institutions, Junagadh. The powdered drugs of selected plant materials were evaluated for physicochemical parameters including total ash, acid-insoluble ash, water-soluble ash, sulphated ash, and extractive values using standard procedures.

2.2.4 Isolation of Cassia roxburghii Gum

Collection of seeds → Size reduction → Powdering → Soaking in water for one day → Extraction by filtration → Centrifugation → Drying of gum → Passed through sieve No. 100.

2.3 Identification of Drug

2.3.1 Preparation of Calibration Curve of Labetalol Hydrochloride

Standard Calibration Curve of Labetalol hydrochloride in 0.1 N HCl: 100 mg of Labetalol hydrochloride was accurately weighed and dissolved in 100 ml of 0.1 N HCl to obtain a concentration of 1 mg/ml (1000 µg/ml). 10 ml of this solution was diluted to 100 ml with 0.1 N HCl (100 µg/ml) as stock solution. The stock solution was subsequently diluted with 0.1N HCl to obtain a series of dilutions containing 5, 10, 15, 20, 25, 30, and 35 µg/ml. The absorbance of the above dilutions was measured at 302 nm by UV-Spectrophotometer with 0.1N HCl as blank. Linearity was assessed from the correlation coefficient (R^2) determined by least-square linear regression analysis.

2.4 Compatibility Studies (FTIR)

An IR spectra-matching approach was used for detection of any possible chemical interaction between drug and polymer. A physical mixture of drug and polymer was prepared and mixed with an appropriate quantity of potassium bromide. About 100 mg of the mixture was compressed to form a transparent pellet using a hydraulic press at 6 tons pressure and scanned from 4000 to 400 cm^{-1}. The IR spectrum of the physical mixture was compared with those of pure drug and polymers to detect any appearance or disappearance of characteristic peaks.

2.5 Differential Scanning Calorimetry (DSC)

The thermal behavior of Labetalol hydrochloride was examined by DSC. An accurately weighed sample of Labetalol hydrochloride (5 mg) was run at a scanning rate of 10°C/min over a temperature range of 150 to 300°C. The DSC thermogram was recorded and reported.

2.6 Preformulation Studies

Prior to development of the dosage form, certain fundamental physical and chemical properties of the drug candidate and

excipients were determined. The preformulation parameters including bulk density, tapped density, compressibility index, and Hausner's ratios were determined as per IP procedure.

2.7 Formulation of Labetalol HCl SR Matrix Tablets

Sustained release tablets of Labetalol hydrochloride were prepared by wet granulation using different natural polymers – Aloe barbadensis, Dioscorea Alata, and Xanthan gum – individually and in combination. Granules were prepared with varying proportions of these polymers with drug. Labetalol HCl was sieved through sieve No. 60. MCC was used as diluent and magnesium stearate as glidant/lubricant. Polyvinylpyrrolidone (PVP K-30) in isopropyl alcohol was added as granulating agent to obtain a coherent mass. The wet granules were dried at room temperature and sieved through sieve No. 24, then mixed with magnesium stearate and compressed. The tablet blend (approximately 350 mg) was compressed at 1.5N force using 16×8 mm concave punches.

Table 5: Formulation of Labetalol HCl SR Matrix Tablets (Trial Batches) — see below

2.8 Optimization Using 2^3 Full Factorial Design

A 2-level, 3-factor full factorial design was created using the conventional technique. The amount of Aloe barbadensis (X1), amount of Dioscorea Alata (X2), and amount of Xanthan gum (X3) were chosen as independent variables. Drug release at 4 hr and 12 hr were selected as dependent variables. All other formulation and processing parameters were maintained constant.

Table 6: Variables in full factorial design

Form. Code	X1 = Aloe barbadensis	X2 = Dioscorea Alata	X3 = Xanthan gum
F1	-1	-1	-1
F2	1	-1	-1
F3	-1	1	-1
F4	1	1	-1
F5	-1	-1	1
F6	1	-1	1
F7	-1	1	1
F8	1	1	1

Table 7: Factor combinations for sustained release matrix tablet

Independent Variable	Low (-1)	Medium (0)	High (+1)
Aloe barbadensis (X1)	30	40	50
Dioscorea Alata (X2)	15	17.5	20
Xanthan gum (X3)	10	12.5	15
Drug release at 4 hrs			
Drug release at 12 hrs			

2.9 Post-Compression Parameters

Physical parameters including thickness, diameter, hardness, friability, weight variation, and uniformity of drug content were evaluated to assess tablet quality and consumer acceptability.

2.10 In Vitro Drug Release Study

In vitro drug release studies were carried out using USP XXII Dissolution Apparatus Type II (Electrolab, Mumbai, India) at 50 rpm. The dissolution medium consisted of 900 ml of Phosphate Buffer pH 6.8 maintained at 37 ± 0.5°C. The drug release at different time intervals was measured using a UV-Visible spectrophotometer (Shimadzu-1800, Mumbai) at 302 nm. The study was performed in triplicate. Volume withdrawn and replaced: 5 ml every 1 hour. Duration: 12 hours.

2.11 Similarity and Difference Factor Calculation

The similarity factor (f2) was defined by CDER, FDA, and EMEA as the logarithmic reciprocal square root transformation of one plus the mean squared difference in percent dissolved between test and reference release profiles. The difference factor (f1) describes the relative error between two dissolution profiles.

Table 8: Similarity factor f2 and its significance

Sr.	Similarity Factor (f2)	Significance
1	< 50	Test and standard profiles are dissimilar
2	50–100	Test and standard profiles are similar
3	100	Test and standard profiles are identical
4	> 100	The equation yields a negative value

2.12 Kinetic Analysis

The results of the in vitro release profiles were analyzed using the following kinetic models: Zero-order kinetic model – cumulative % drug released vs. time; First-order kinetic model – log cumulative % drug remaining vs. time; Higuchi's model – cumulative % drug released vs. square root of time; Korsmeyer-Peppas model – log cumulative % drug released vs. log time.

2.13 Stability Studies

Selected formulations were stored at different storage conditions: 25°C ± 2°C/60% ± 5% RH, 30°C ± 2°C/65% ± 5% RH, and 40°C ± 2°C/75% ± 5% RH for 90 days. Samples were withdrawn at 15-day intervals and checked for physical changes, hardness, friability, drug content, and percentage drug release.

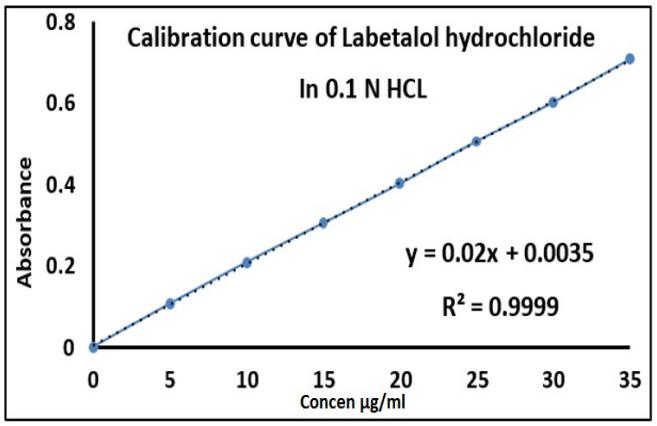
3. RESULTS AND DISCUSSION

3.1 Calibration Curve of Labetalol Hydrochloride

The standard calibration curve of Labetalol hydrochloride in 0.1 N HCl showed good linearity (λmax 302 nm). The correlation coefficient was calculated by linear regression analysis and confirmed the suitability of the method for drug quantification. Results are presented in Table 9.

Table 9: Standard graph of Labetalol hydrochloride in 0.1 N HCl (λmax 302 nm)

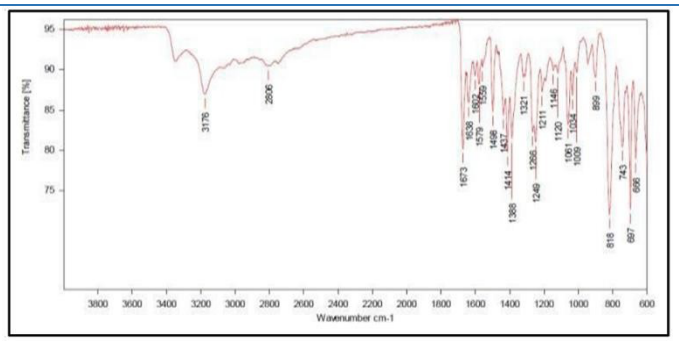
Sr.	Conc. (mcg/ml)	Absorbance Mean ± SD
1	0.00	0.000±0.000
2	5.00	0.104±0.001
3	10.00	0.207±0.002
4	15.00	0.306±0.002
5	20.00	0.405±0.002
6	25.00	0.506±0.003
7	30.00	0.702±0.003
8	35.00	0.805±0.003



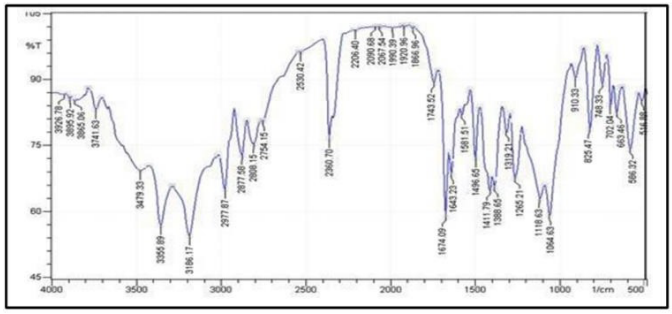
[Figure 3: Standard calibration curve of Labetalol hydrochloride in 0.1 N HCl – to be inserted here]

3.2 FTIR Study

Infrared spectroscopy is one of the most powerful analytical techniques for the determination of functional groups. IR spectra of Labetalol hydrochloride and its formulations were obtained by the KBr pellet method using a Shimadzu FTIR series model-8400S spectrometer to rule out drug-carrier interaction during the formulation process. The IR spectrum of the optimized formulation F8 showed no significant changes in the characteristic peaks of Labetalol HCl, confirming compatibility between drug and excipients.



[Figure 4: IR Spectra of Labetalol hydrochloride (Pure drug) – to be inserted here]



[Figure 5: IR Spectrum of Drug with polymer mixture (Optimized formulation F8) – to be inserted here]

3.3 Preformulation Studies

Precompression parameters including angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratios were studied to evaluate the flowability and compressibility of the powder formulations. Results are summarized in Table 10.

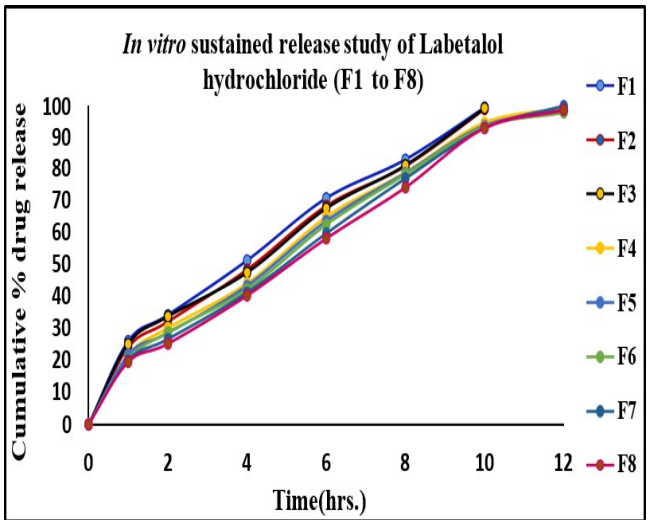
Table 10: Preformulation study results (Trial batches) — see full table below

3.4 Post-Compression Parameters

All tablet batches were evaluated for post-compression parameters. The average weight of tablet formulations was within the range of 348.01–350.40 mg, and the measured hardness of tablets ranged between 6.20–7.40 kg/cm². The percentage drug content of all batches was found to be between 95.25% and 98.80%, within acceptable limits. Results are compiled in Table 11 (below).

3.5 In Vitro Drug Release

Cumulative percentage drug release from Labetalol HCl sustained release tablets is presented in Table 12 (below). The polymer concentration had a significant effect on the drug release profile. Batches LH1, LH3, LH5, and LH7 showed more than 75% drug release after 12 hours. Batches LH1 and LH5 exhibited initial high release, releasing approximately 80% of drug after 6 hours. The average concentration of Aloe barbadensis (30–50 mg), Dioscorea Alata (15–20 mg), and Xanthan gum (10–15 mg) showed a promising approach for the development of a sustained release dosage form of Labetalol HCl.



[Figure 6: In vitro drug release study of Labetalol hydrochloride – to be inserted here]

3.6 Optimization Using Full Factorial Design

A statistical model incorporating interactive and polynomial terms was used to evaluate the responses. A 2^3 randomized full factorial design was utilized, evaluating three factors at two levels each, resulting in eight experimental trial combinations. The polynomial equations obtained are:

$$Y1 = +18.90 - 0.14X1 - 0.03X2 - 0.54X3 + 0.87X1X2 + 0.762X2X3 + 0.90X3X1 + 1.4X1^2 - 0.6X2^2 - 0.10X3^2$$

$$Y2 = +10.42 - 0.67X1 - 0.210X2 - 0.18X3 + 2.67X1X2 + 1.804X2X3 + 2.76X3X1 + 1.98X1^2 - 1.56X2^2 - 0.76X3^2$$

The concentrations of Aloe barbadensis (X1), Dioscorea Alata (X2), and Xanthan gum (X3) had a substantial impact on drug release at 12 hours. Drug release and Aloe barbadensis (X1) showed an inverse association; as concentration rose from 30 mg to 50 mg, drug release at 12 hours decreased, likely due to greater gel-forming capacity creating a more viscous matrix that retards drug diffusion. Conversely, Dioscorea Alata (X2) positively impacted drug release; increasing its concentration from 15 mg to 20 mg improved drug release, possibly due to enhanced hydration or faster matrix erosion. Similarly, Xanthan gum (X3), particularly at higher concentrations (15 mg), provided a well-balanced gel matrix promoting prolonged drug diffusion without significantly impairing release.

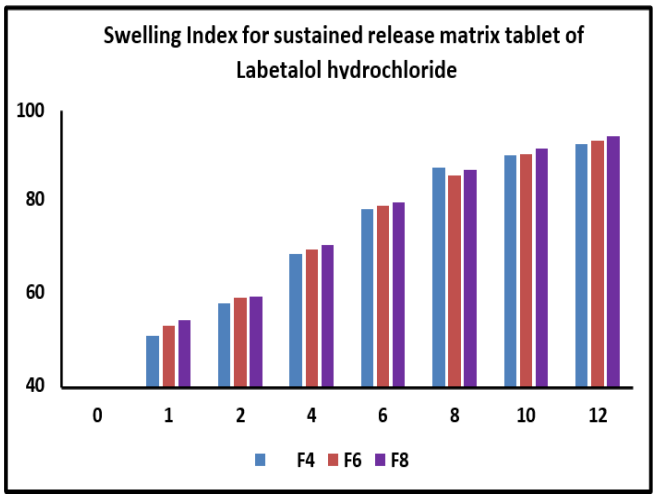
Precompression and post-compression parameters of the factorial design batches are summarized in Tables 13 and 14 (below).

3.7 Swelling Study

Drug release profiles are dependent upon the swelling behavior of the tablets. Swelling index increased proportionately with the rate of hydration. As concentrations of Aloe barbadensis (X1), Dioscorea Alata (X2), and Xanthan gum (X3) increased, swelling index increased proportionally. Factorial batch F8 containing 50 mg of Aloe barbadensis, 20 mg of Dioscorea Alata, and 15 mg of Xanthan gum swelled 90.80% after 12 hours, which was higher than all other formulations.

Table 15: Swelling index for sustained release matrix tablet of Labetalol HCl

Time (hr)	F4	F6	F8
0	0.00	0.00	0.00
1	18.70	22.50	24.13
2	30.59	32.29	33.00
4	48.10	49.70	51.35
6	64.54	65.56	66.95
8	79.20	76.54	78.60
10	83.65	84.39	86.15
12	88.10	89.04	90.80



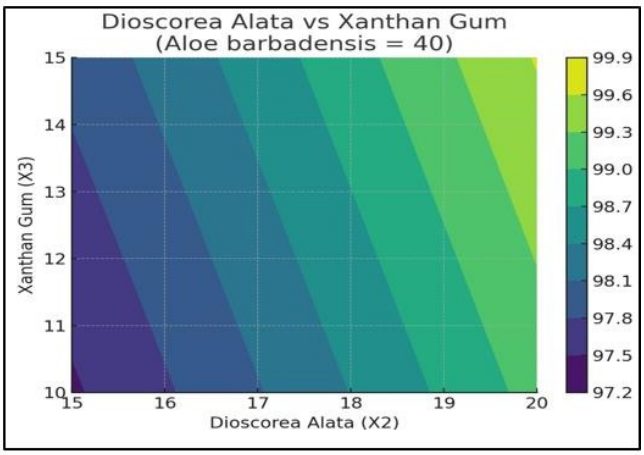
[Figure 7: Swelling index for sustained release matrix tablet of Labetalol HCl – to be inserted here]

3.8 ANOVA for Response Drug Release at 12 hr

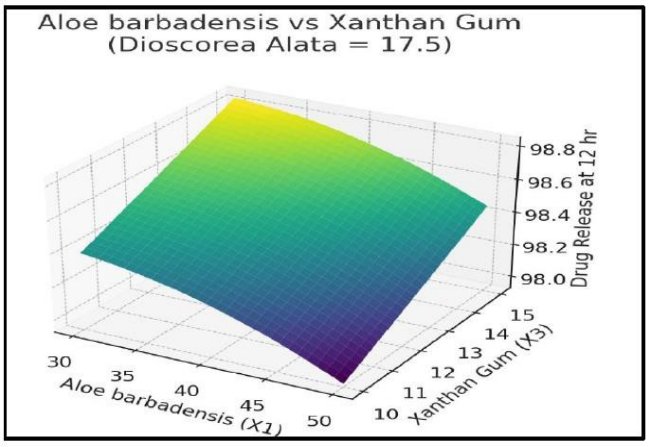
Analysis of variance was performed for the drug release response at 12 hours. The model was found to be significant with an R^2 value of 0.9840, indicating a good fit. Results are summarized in Table 16.

Table 16: Analysis of variance for response drug release at 12 hr

Source	Sum of Sq.	df	Mean Sq.	F Value	P Value	Significance
Model	303407	5	75685.2	51.16	0.0039	Significant
X1	3.546E+023	1	3.54E+005	223.0	0.003	Significant
X2	11832.5	1	10354.5	5.34	0.001	Significant
X3	4952.10	1	54621.3	3.89	0.004	Significant
Residual	1194.6	3	321.18	–		–



[Fig No. 8: Contour plot showing the effect of Dioscorea Alata(X2) and Amount of Xanthan gum (X3) on drug release at 12hr]



[Fig No. 12: Response surface plot showing the effect of Amount of Aloe barbedensis gum(X1) and Amount of Xanthan gum (X3) on drug release at 12 hr]

3.9 Stability Study

Stability study of the optimized formulation F8 was carried out for one month (30 days). The results showed no significant change in hardness, thickness, friability, % drug content, swelling index, or drug release profile (Tables 17 and 18). This confirms that the optimized batch F8 is stable and reproducible.

Table 17: Stability study of Batch F8 – Post-compression parameters

Parameters	Initial	After 30 days
Average Weight (mg)	350.10±4.5	349.20±3.1
Hardness (kg/cm²)	7.40±0.68	7.38±0.20
Thickness (mm)	3.43±0.014	3.43±0.20
% Friability	0.22	0.24
% Drug Content	97.05±0.058	96.80±0.10
Swelling Index after 12 hr	90.80±0.04	91.10±0.08

Table 18: Stability study of Batch F8 – In vitro drug release

Time (hr)	Initial	After 30 days
0	0	0
1	20.10	19.85
2	26.67	25.65
4	41.22	41.07
6	59.75	58.60
8	76.95	75.40
10	92.70	91.80
12	99.70	98.80

4. CONCLUSION

Labetalol hydrochloride is used in the treatment of hypertension and has a short half-life with extensive first-pass metabolism. In the present study, matrix tablets of Labetalol HCl were successfully prepared by wet granulation using Aloe barbadensis, Dioscorea Alata, and Xanthan gum as natural polymers. The purpose of this research was to produce a sustained-release matrix tablet that exhibits higher patient compliance, decreases adverse effects, and enhances oral bioavailability.

Out of eight formulations of sustained release matrix tablets, only formulations F4–F8 were able to maintain the release of Labetalol HCl for 12 hours. Formulation F8, containing 50 mg of Aloe barbadensis, 20 mg of Dioscorea Alata, and 15 mg of Xanthan gum, was able to swell 90.80% more after 12 hours compared to other formulations and is therefore considered the optimized formulation. The drug transport mechanism follows Fickian diffusion (Korsmeyer-Peppas model), and the stability study confirmed no significant change in drug release profile, establishing F8 as a stable and reproducible formulation.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

Table 5: Formulation of Labetalol HCl SR Matrix Tablets (Trial Batches)

Ingredients (mg)	LH1	LH2	LH3	LH4	LH5	LH6	LH7	LH8
Labetalol HCl	100	100	100	100	100	100	100	100
Aloe barbadensis	30	40	50	60	30	40	50	60
Dioscorea Alata	15	20	15	20	15	20	15	20
Xanthan gum	10	10	10	10	15	15	15	15
PVP K-30	15	15	15	15	15	15	15	15
Isopropyl alcohol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Mg. Stearate	7	7	7	7	7	7	7	7
MCC PH102	169.5	154.5	149.5	134.5	164.5	149.5	144.5	129.5
Total weight (mg)	350	350	350	350	350	350	350	350

Table 10: Results of preformulation studies of Labetalol HCl SR Matrix Tablets (Trial batches)

Formulation Code	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratios
LH1	35°18'	0.635	0.810	21.60	1.27
LH2	34°07'	0.622	0.826	24.69	1.32
LH3	35°16'	0.607	0.810	25.06	1.33
LH4	33°09'	0.621	0.840	26.07	1.35
LH5	32°19'	0.603	0.810	25.06	1.33
LH6	33°71'	0.625	0.839	21.15	1.26
LH7	33°02'	0.664	0.881	24.29	1.32
LH8	35°13'	0.602	0.810	25.05	1.32

Table 11: Results of evaluation of trial batches of Labetalol HCl SR Matrix Tablets

Batch	Weight Variation (mg)	Friability (%)	Diameter (mm)	Thickness (mm)	Hardness (Kg/cm²)	Drug Content (%)
LH1	351.16±5.8	0.20	7.20±0.10	3.38±0.089	5.50±0.25	98.11±3.25
LH2	350.31±5.5	0.21	7.28±0.05	3.33±0.014	5.65±0.48	98.80±2.01
LH3	349.26±6.4	0.22	7.21±0.08	3.35±0.168	5.70±0.35	99.23±3.85
LH4	350.40±6.6	0.23	7.20±0.05	3.35±0.212	5.90±0.26	98.90±2.74
LH5	348.93±7.4	0.20	7.22±0.07	3.37±0.078	6.20±0.56	98.38±4.45
LH6	349.35±4.6	0.21	7.2±0.05	3.39±0.235	6.30±0.26	97.88±5.45
LH7	352.01±4.2	0.23	7.22±0.05	3.30±0.245	6.40±0.26	97.16±4.74
LH8	349.65±6.6	0.24	7.22±0.03	3.31±0.114	6.50±0.78	98.51±4.68

Table 12: Cumulative percentage drug release from Labetalol HCl sustained release tablets

Time (hr)	LH1	LH2	LH3	LH4	LH5	LH6	LH7	LH8
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	33.03	16.50	15.05	13.40	27.13	18.22	16.55	14.04
2	60.09	25.50	26.27	27.60	56.69	25.07	27.90	25.10

Time (hr)	LH1	LH2	LH3	LH4	LH5	LH6	LH7	LH8
4	82.24	35.25	37.10	38.50	77.24	31.03	38.07	32.81
6	87.84	43.30	45.10	44.02	80.84	35.99	44.75	38.03
8	89.05	55.10	57.20	53.72	82.05	47.30	62.22	47.86
10	89.50	64.20	71.10	64.53	85.06	58.29	72.62	56.17
12	89.10	71.50	77.10	69.58	87.58	68.62	78.90	63.90

Table 13: Precompression parameters of 2^3 factorial design batch of Labetalol HCl

Formulation	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratios
F1	25°18'	0.505	0.610	17.25	1.23
F2	28°73'	0.426	0.505	20.41	1.24
F3	30°23'	0.506	0.705	25.04	1.28
F4	32°12'	0.564	0.674	25.06	1.31
F5	31°61'	0.560	0.721	23.06	1.30
F6	29°07'	0.450	0.530	26.51	1.19
F7	34°12'	0.547	0.670	25.58	1.34
F8	30°16'	0.450	0.550	24.56	1.32
F9	33°05'	0.578	0.675	26.19	1.30

Table 14: Post-compression parameters of 2^3 factorial design batch of Labetalol HCl

Form.	Diameter (mm)±SD	Thickness (mm)±SD	Weight Variation (mg)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)
F1	7.05±0.016	3.45±0.212	350.40±5.6	6.20±0.56	0.32±0.007	95.25±0.04
F2	7.00±0.002	3.47±0.078	348.93±7.4	6.50±0.26	0.30±0.005	96.11±0.037
F3	7.03±0.007	3.49±0.235	349.65±6.6	6.60±0.26	0.31±0.031	97.64±0.07
F4	7.01±0.002	3.45±0.245	348.01±5.2	6.80±0.78	0.57±0.016	95.27±0.087
F5	7.05±0.015	3.41±0.114	349.95±5.6	6.80±0.68	0.30±0.09	98.47±0.058
F6	7.03±0.010	3.45±0.212	349.69±9.6	7.30±0.68	0.25±0.01	97.10±0.073
F7	7.05±0.016	3.49±0.124	349.32±3.6	7.30±1.25	0.25±0.00	98.80±0.08
F8	7.10±0.015	3.43±0.014	350.10±4.5	7.40±0.68	0.22±0.09	97.05±0.058
F9	6.97±0.010	3.45±0.168	350.96±6.4	6.70±1.25	0.19±0.01	97.15±0.073

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