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Formulation and Evaluation of Sublingual Tablet of Eplerenone

Shivang B. Chosaliya, Suraj R. Chauhan, Jitendra O. Bhangale
Smt. N. M. Padalia Pharmacy College, Ahmedabad, Gujarat, 382210, India.
*Corresponding Author E-mail: **jitu2586@gmail.com**

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ABSTRACT:
The present study was aimed at the formulation and evaluation of sublingual tablets of eplerenone using natural disintegrants to enhance its bioavailability and therapeutic effectiveness. Eplerenone, a selective aldosterone antagonist used in the management of hypertension, belongs to BCS class II and undergoes extensive first-pass metabolism, resulting in reduced oral bioavailability. To overcome these limitations, sublingual tablets were developed to facilitate rapid absorption through the sublingual mucosa and bypass hepatic metabolism. The tablets were formulated by direct compression using natural disintegrants such as chitosan and karaya gum. Preformulation studies, including melting point determination and UV spectrophotometric analysis, confirmed the identity and purity of the drug, with a λ_{max} observed at 242 nm. FTIR studies indicated no significant interaction between the drug and excipients, confirming compatibility. The prepared formulations were evaluated for pre- and post-compression parameters. All batches exhibited satisfactory flow properties, acceptable hardness, low friability, and uniform weight variation within pharmacopeial limits. The wetting time and *in vitro* disintegration time were found to be in the range of 21–39 sec and 24–41 sec, respectively, indicating rapid tablet disintegration. *in vitro* dissolution studies demonstrated that drug release increased with higher concentrations of disintegrants. Among all formulations, batch E6 (Karaya Gum=15 mg) showed optimal performance with 99.72% drug release within 10 minutes and the shortest disintegration time of 24.67 ± 0.58. Stability studies confirmed that the optimized formulation remained stable under accelerated conditions. Thus, the developed sublingual tablets of eplerenone using natural disintegrants offer a promising approach for rapid drug delivery and improved bioavailability.

INTRODUCTION:

Eplerenone is a selective aldosterone antagonist that blocks mineralocorticoid receptors within the renin–angiotensin–aldosterone system (RAAS), thereby reducing blood pressure and preventing complications such as stroke, myocardial infarction, and renal dysfunction. However, its therapeutic effectiveness is limited by pharmacokinetic constraints, including a short elimination half-life (4–6 hours), classification as a BCS class II drug (low solubility and high permeability), and moderate oral bioavailability (~69%) due to extensive hepatic first-pass metabolism.[1,2]

These limitations necessitate the development of an alternative delivery system to enhance its bioavailability and onset of action. The sublingual route offers a promising approach, as it enables rapid drug absorption directly into the systemic circulation through the rich vascular network beneath the tongue, thereby bypassing hepatic first-pass metabolism. Although various formulations of eplerenone, such as conventional tablets, fast disintegrating tablets, and mucoadhesive buccal systems, have been explored, limited research has been reported on its sublingual delivery. Therefore, the present study aims to develop sublingual tablets of eplerenone to improve its bioavailability, ensure rapid onset of action, and enhance overall therapeutic efficacy.[3]

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MATERIALS AND METHODS:

Materials: Eplerenone was procured from Cadila Pharmaceuticals Ltd (Ahmedabad, India) as gift sample. MCC, Karaya gum, Chitosan, Mannitol, Talc, Magnesium stearate was purchased by Chemdyes Corporation, India.

Formulation method for sublingual tablet: Sublingual tablets of Eplerenone were prepared by the direct compression method in which all ingredients were accurately weighed according to the formulation design and passed through a 44# sieve to ensure uniform particle size distribution. Eplerenone was blended with natural disintegrant, MCC, Mannitol Subsequently, Talc, Magnesium stearate were incorporated and gently mixed to improve flow and lubrication. The final blend was compressed into sublingual tablets using 8 mm flat round punches on a Rimek multi-rotary 16-station tablet compression machine, and the prepared tablets were evaluated for various physicochemical parameters to ensure suitability for sublingual administration.[4,5] All formulation compositions are listed in **Table 1**.

Table 1: Formulation Design of Sublingual Tablets[6-10]

Ingredients (mg)	E1	E2	E3	E4	E5	E6
Eplerenone	25	25	25	25	25	25
MCC	30	30	30	30	30	30
Chitosan	5	10	15	-	-	-
Karaya Gum	-	-	-	5	10	15
D-Mannitol	50	45	40	50	45	40
Magnesium strearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Tablet weight (mg)	120	120	120	120	120	120

PREFORMULATION STUDIES OF EPLERENONE:

Identification of Eplerenone by melting point determination:

Melting point of Eplerenone was measured by melting point apparatus. Minimum amount of drug was placed in a thin-walled capillary tube closed at one end. This capillary was then mounted in a melting point apparatus with thermometer and then their temperature range over which Eplerenone melts is measured. The readings were taken in triplicate.[11]

Estimation of Eplerenone by UV Spectroscopy: Standard stock solution of Eplerenone was prepared by dissolving 10 mg of Eplerenone in 100 ml Phosphate buffer pH 6.8, which make the stock solution of concentration of 100 µg/ml. For determination of λ_{max}, stock solution was scanned between 200-400 nm against Phosphate buffer pH 6.8 as a blank in the UV-Visible spectrophotometer. Working solution of concentration 10, 20, 30, 40 and 50 ppm were prepared by pipette outing 1, 2, 3, 4 and 5 ml respectively from the stock solution of 100 ppm and diluted up to 10 ml in volumetric flask. Absorbance of working solutions was measured in triplicate at λ_{max} 242 nm against Phosphate buffer pH 6.8 as a blank. [12]

Determination of drug by FTIR: FTIR was performed for determination of Eplerenone and was estimated for standard FTIR peaks. FTIR spectroscopy of pure drug and physical mixture of drug and excipients was carried out to check the compatibility of drug and excipients.[13]

Pre-compression Parameters:

Bulk density: Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume and weight of the powder was determined. [14]

$$\text{Bulk density} = \frac{\text{Mass of Powder (gm)}}{\text{Bulk volume of Powder (ml)}}$$

Tapped density: The measuring cylinder containing a known mass of blend was tapped for 100 times. The minimum volume occupied in the cylinder and weight of the blend was measured. [14]

$$\text{Tapped density} = \frac{\text{Mass of Powder (gm)}}{\text{Tapped volume of Powder (ml)}}$$

Compressibility Index: Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size distribution of the powder. Tapped density and Bulk density measurements can be used to estimate the compressibility of a material. [15]

$$\% \text{ Carr's Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} X\ 100$$

Hausner's ratio: The Hausner's ratio is used for estimation of the flow property of either particles or granules. Hausner's ratio is the ratio of tapped density to bulk density of particles or granules.[15] Its value less than 1.25 indicates excellent flow of particles and value more than 1.25 indicates poor flow property. The Hausner's ratio of the granules was determined by the equation.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Angle of repose: Angle of repose has been defined as the maximum angle possible between the surface of pile of powder and horizontal plane. Angle of repose of different formulations was measured according to fixed funnel standing method. The granules mass was allowed to flow out of the funnel orifice on a plane paper kept on the horizontal surface. This forms a pile of granules on the paper. The Angle of repose is calculated by the equation. [15]

$$\text{Tan}\,\theta = \frac{\text{Height of pile (h)}}{\text{radius of pile (r)}}$$

Post Compression Parameters:

Thickness: Thickness of tablets were measured by Digi-MaticVernier calipers. 3 tablets were randomly collected and their thickness were measured by placing between two arms of Vernier calipers.[16]

Hardness: The hardness of tablets is an indication of its strength. Measuring the force required to break the tablet across tests it. The crushing strength of tablets was measured by using Monsanto type hardness tester. The hardness of the sublingual tablets should typically range between 2 to 5 kg/cm² to ensure adequate mechanical strength while allowing rapid dissolution under the tongue.[16]

Weight Variation: 20 tablets selected at random were weighed and the average weight was calculated.[16]

Friability test: The friability of tablets was measured by Roche type friabilator. 20 tablets were initially weighed and then tablets were placed in friabilator at 25 rpm for 4 min then tablets were deducted and weighed again. Loss in weight should not be more than 1 %. Friability determined by using following equation.[17]

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Drug content: 10 tablets were weighed and average weight was calculated. All 10 tablets were crushed in mortar. The powder equivalent to 25 mg of Eplerenone was dissolved in small quantity of methanol and then made up to 10 ml with phosphate buffer 6.8. The drug solution was filtered through Whatman filter paper. The sample was analyzed for drug content by UV Spectrophotometry at 242 nm after suitable dilutions.[18]

Wetting time: Six circular tissue papers of 10 cm diameter were placed in a petridish. 10 ml of phosphate buffer (pH 6.8) containing amaranth dye was added to petridish. A tablet was carefully placed on the surface of tissue paper. Time required for water to reach the upper surface of tablet was noted as a wetting time.[19]

***in vitro* Disintegration test:** This test performed on six tablets using digital tablet disintegration test apparatus. 500 ml Phosphate buffer (pH 6.8) at 37 ± 0.5 °C was used as a disintegration media and time in sec. was recorded for complete disintegration of tablet with no residue remaining in apparatus.[19]

***in vitro* Drug release study:** *in vitro* drug release of Eplerenone Sublingual Tablets was determined by USP type II (paddle type) dissolution apparatus. This test was performed using 900 ml of phosphate buffer (pH 6.8) at 37 ± 0.5 °C at 50 rpm. 5 ml samples were withdrawn 5 min of time interval and the same quantity of sample was replaced

with fresh dissolution media. The sample was filtered through 0.45 µm membrane filter. Absorbance of these samples was analyzed by using UV spectrophotometer 242 nm.[20]

Stability study: In the present study, stability study of optimized batch was carried out at 40 ± 2°C/ 75 ± 5% RH for time period of 1 month by wrapping the formulation in aluminum foil to prevent the formulation from exposure to light under the as prescribed by ICH guidelines for accelerated stability study. After completion of 30 days tablets were evaluated for Hardness, Weight variation, Drug content, Wetting time, *in vitro* Disintegration time and *in vitro* Drug release study. [20]

RESULTS AND DISCUSSION

Melting Point: Melting point determination is one of the popular techniques used to identify drug using melting point apparatus and melting point of Eplerenone was found in the range of 241°-243°C. Reported melting point of Eplerenone is 240-244 °C and is thus similar to the melting point of Eplerenone. Results are depicted in table 2.

Table 2: Melting point of Eplerenone.

Sr. No.	Reported Melting Point	Observed Melting point
1.	241°-243°C	240°-242°C
2.	241°-243°C	241°-244°C
3.	241°-243°C	241°-243°C

6.1.2 Estimation of drug by UV spectra of Eplerenone

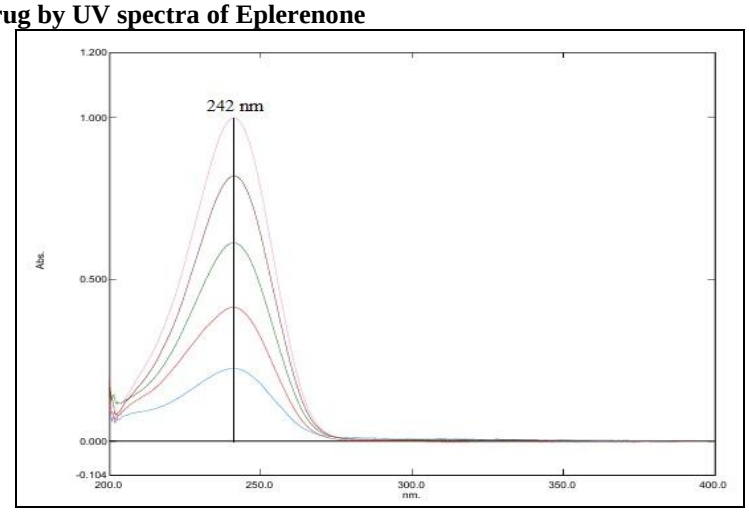

Figure 1: UV Spectra of Eplerenone

The absorbance of Eplerenone in Phosphate buffer pH 6.8 was scanned between 200–400 nm by UV-Visible spectrophotometer. The spectrum of Eplerenone showed 242 nm at λ_{max} as shown in figure 1. Calibration curve of Eplerenone is constructed in Phosphate buffer pH 6.8 From stock solution of Eplerenone, working solution of concentration range i.e., 10, 20, 30, 40 and 50 ppm were prepared in Phosphate buffer pH 6.8. Absorbance of prepared working solutions were measured at λ_{max} 242 nm against Phosphate buffer pH 6.8 as a blank in UV–Visible Spectrophotometer. Calibration curve of prepared working solutions of Eplerenone was constructed by plotting a graph between concentration and absorbance (figure 2) from the data are shown in table 3.

Table 3: Absorbance of different concentration of Eplerenone in phosphate buffer at pH 6.8

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance ± S. D.
		I	II	III	
1.	10	0.223	0.221	0.224	0.223 ± 0.002
2.	20	0.411	0.413	0.409	0.411 ± 0.002
3.	30	0.61	0.608	0.613	0.610 ± 0.003
4.	40	0.818	0.821	0.815	0.818 ± 0.003
5.	50	1.003	1.001	0.997	1.000 ± 0.003

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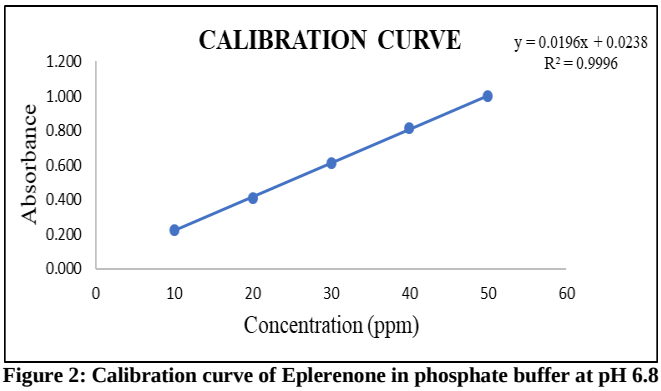

Figure 2: Calibration curve of Eplerenone in phosphate buffer at pH 6.8

6.1.3. FT-IR Study of Eplerenone

FT-IR spectra of drug was obtained by FT-IR spectrophotometer. Required quantity of drug was kept directly in the sample compartment of FT-IR and scanned in the range of 400-4000 cm^{-1}. The spectrum of pure drug is shown in figure 3. Similarly the drug-excipient combination was scanned and the resultant spectrum is shown in figure 4.

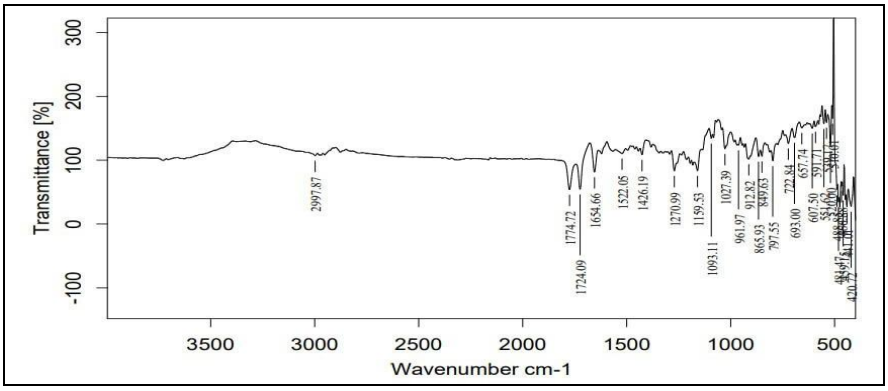

Figure 3: IR spectra of Pure drug Eplerenone

The FTIR spectrum of pure eplerenone exhibited characteristic absorption bands consistent with its reported chemical structure. A prominent peak observed around 2957 cm^{-1} corresponds to aliphatic C–H stretching vibrations. The strong and sharp bands at approximately 1742 cm^{-1} and 1724 cm^{-1} are indicative of ester and lactone carbonyl (C=O) stretching, which are key functional groups in eplerenone. Additional peaks at ~1646 cm^{-1} and 1562 cm^{-1} can be attributed to C=C stretching of the conjugated system, while bands in the region of 1450–1370 cm^{-1} represent C–H bending vibrations. The peaks observed near 1270 cm^{-1} and 1093 cm^{-1} are associated with C–O stretching, and those below 1000 cm^{-1} correspond to fingerprint region vibrations, confirming the structural integrity of the drug. These characteristic peaks align well with reported literature, confirming the identity of eplerenone.

6.1.4. Eplerenone with excipient by FTIR spectra

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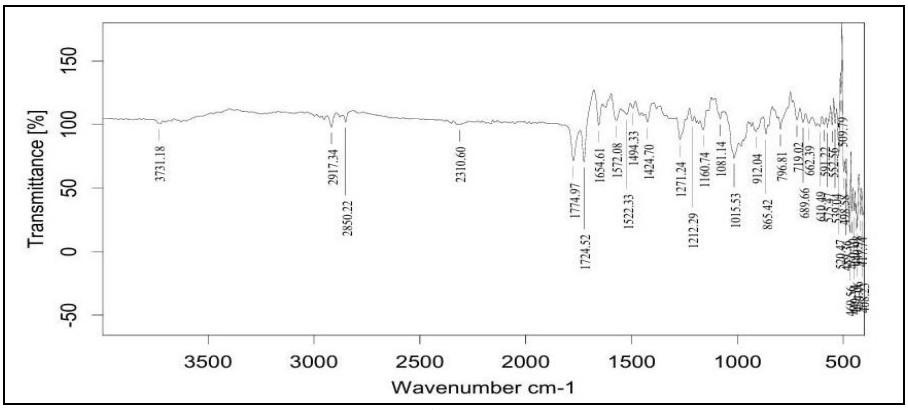

Figure 4: IR Spectra of Eplerenone with excipients

In the FTIR spectrum of the drug–excipient formulation, all major characteristic peaks of eplerenone were retained with negligible shifts in their positions and the spectra is shown figure 4. The carbonyl stretching peaks remained prominent around 1747 cm^{-1} and 1724 cm^{-1}, while other functional group peaks showed minimal variation in intensity and position. No disappearance of characteristic peaks or emergence of new peaks was observed. This indicates the absence of any significant chemical interaction between the drug and excipients. The preservation of key functional group vibrations suggests that the drug remains structurally stable within the formulation, confirming compatibility and suitability of the selected excipients for formulation development.

Evaluation of Sublingual Tablet of Eplerenone:

Precompression Parameters: The precompression parameters of all formulation batches (E1–E6) demonstrated satisfactory flow and compressibility characteristics, indicating suitability for direct compression as shown in table 4. The **bulk density** of the powder blends was found to range from 0.41 ± 0.00 to 0.50 ± 0.01 g/ml, while the **tapped density** ranged from 0.42 ± 0.01 to 0.52 ± 0.01 g/ml. The relatively close values between bulk and tapped densities suggest minimal densification upon tapping, reflecting good packing ability of the blends.

Hausner's ratio values for all batches were observed between 1.03 ± 0.01 and 1.04 ± 0.01, which fall well within the acceptable range (<1.25), indicating excellent flow properties. Similarly, the **Carr's index** values ranged from 2.44 ± 1.04% to 3.77 ± 0.07%, which correspond to excellent compressibility and further confirm good flow behavior of the powder blends.

The **Angle of repose** for all formulations was found in the range of 25.23 ± 0.87° to 27.62 ± 2.22°, suggesting good flowability as per standard limits. Among all batches, E6 exhibited the lowest angle of repose, indicating comparatively better flow characteristics.

Overall, the results clearly indicate that all formulation blends possessed good to excellent flow properties and compressibility, making them suitable for uniform die filling and consistent tablet compression during the manufacturing process.

Table 4: Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of Repose data

Batch	Bulk density (gm/ml ± S.D.)	Tapped density (gm/ml ± S.D.)	Hausner's ratio	Carr's index (%)	Angle of repose (°θ)
E1	0.50 ± 0.01	0.52 ± 0.01	1.04 ± 0.01	3.47 ± 1.21	27.62 ± 2.22
E2	0.47 ± 0.01	0.49 ± 0.01	1.03 ± 0.01	3.29 ± 1.16	27.45 ± 2.37
E3	0.42 ± 0.01	0.43 ± 0.00	1.03 ± 0.01	2.91 ± 0.98	26.45 ± 1.27
E4	0.45 ± 0.01	0.47 ± 0.01	1.04 ± 0.00	3.77 ± 0.07	27.36 ± 0.57
E5	0.44 ± 0.00	0.45 ± 0.00	1.03 ± 0.01	2.44 ± 1.04	27.20 ± 1.30
E6	0.41 ± 0.00	0.42 ± 0.01	1.03 ± 0.01	2.84 ± 1.00	25.23 ± 0.87

(n=3)

Post-Compression Parameters: The post-compression evaluation of all formulated batches (E1–E6) indicated that the tablets possessed acceptable physical and mechanical properties in accordance with pharmacopeial standards as shown in table 5 and table 6.

The **thickness** of the tablets was found to be in the range of 1.72 ± 0.02 mm to 1.79 ± 0.01 mm, indicating uniform die filling and consistent compression across all batches.

The **weight variation** of the tablets ranged from 119.05 ± 1.43 mg to 120.05 ± 1.23 mg, which falls within the acceptable limits for a 120 mg tablet as per Indian Pharmacopoeia, confirming uniformity of dosage units.

The **hardness** of the tablets was observed between 2.67 ± 0.29 kg/cm² and 4.67 ± 0.29 kg/cm², suggesting adequate mechanical strength to withstand handling while still allowing rapid disintegration, which is essential for sublingual delivery.

The **friability** values of all batches were found to be between 0.56% and 0.81%, which are well below the pharmacopeial limit of 1%, indicating good resistance to abrasion and mechanical stress. Among all batches, E6 exhibited the lowest friability, reflecting superior mechanical stability.

Overall, the results demonstrate that all formulated tablets exhibited satisfactory post-compression characteristics, ensuring their suitability for further evaluation and confirming the effectiveness of the selected formulation approach.

Table 5: Weight variation, Thickness, Hardness and Friability data

Batch code	Thickness (mm ± S.D.)	Weight variation (mg ± S.D.)	Hardness (kg/cm^2 ± S.D.)	Friability (%)
E1	1.76 ± 0.02	119.05 ± 1.43	4.67 ± 0.29	0.81
E2	1.72 ± 0.02	119.10 ± 1.52	4.33 ± 0.58	0.79
E3	1.77 ± 0.01	119.95 ± 1.61	2.67 ± 0.29	0.61
E4	1.77 ± 0.02	119.25 ± 1.48	4.17 ± 0.29	0.71
E5	1.74 ± 0.01	119.70 ± 1.59	3.00 ± 0.50	0.69
E6	1.79 ± 0.01	120.05 ± 1.23	3.17 ± 0.58	0.56

(n=3)

The evaluation of **wetting time**, *in vitro* disintegration time, and drug content for all formulated batches (E1–E6) demonstrated satisfactory performance of the sublingual tablets. The wetting time was observed in the range of 21.67 ± 1.53 to 39.33 ± 1.53 seconds, indicating rapid penetration of dissolution medium into the tablet matrix. Among all batches, E6 exhibited the shortest wetting time, suggesting efficient action of the disintegrant system.

The ***in vitro* disintegration time** of the tablets ranged from 24.67 ± 0.58 to 41.33 ± 0.58 seconds, which is well within the acceptable limits for sublingual tablets and confirms their rapid disintegration behavior. A decrease in disintegration time was observed with an increase in the concentration of disintegrants, with batch E6 showing the fastest disintegration, making it the most promising formulation.

The **drug content** of all batches was found between 97.57 ± 0.65% and 99.60 ± 0.26%, indicating uniform distribution of the drug within the tablets and compliance with pharmacopeial standards.

Overall, the results indicate that all formulations exhibited rapid wetting and disintegration along with uniform drug content, confirming their suitability for sublingual delivery. Among them, batch E6 demonstrated superior performance and can be considered as the optimized formulation.

Table 6: Wetting time, *in vitro* disintegration time and Drug Content

Batch code	Wetting time (sec. ± S.D.)	*in vitro* disintegration time (sec. ± S.D.)	Drug content (%)
E1	39.33 ± 1.53	41.33 ± 0.58	97.57 ± 0.65
E2	35.67 ± 0.58	36.33 ± 1.15	97.81 ± 0.30
E3	25.33 ± 1.53	27.00 ± 1.00	99.39 ± 0.49
E4	33.33 ± 1.53	36.33 ± 1.53	98.04 ± 0.32
E5	29.33 ± 0.58	32.67 ± 1.53	98.16 ± 0.66
E6	21.67 ± 1.53	24.67 ± 0.58	99.60 ± 0.26

(n=3)

The ***in vitro* drug release** profiles of all formulated batches (E1–E6) demonstrated a rapid and progressive release of eplerenone over a period of 10 minutes, indicating the suitability of the formulations for sublingual delivery as shown in table 7 and figure 5. At the initial time point (2 minutes), drug release ranged from 27.60% to 31.26%, suggesting an immediate onset of dissolution. As time progressed, a consistent increase in drug release was observed across all batches, reflecting efficient disintegration and drug diffusion. At 6 minutes, the drug release varied

between 55.94% and 72.23%, indicating that more than half of the drug was released within a short duration. Further, at 8 minutes, cumulative drug release reached up to 93.41% in batch E6, demonstrating its superior performance compared to other batches. By the end of 10 minutes, all formulations showed substantial drug release, ranging from 85.12% to 99.72%. Among all batches, E6 exhibited the highest drug release (99.72%) within 10 minutes, followed by E3 (97.69%) and E5 (94.26%). This enhanced release profile can be attributed to the optimal concentration of disintegrants, which facilitated rapid tablet disintegration and drug dissolution. Overall, the results indicate that all formulations provided rapid drug release; however, batch E6 showed the most efficient release pattern and was identified as the optimized formulation for sublingual delivery of eplerenone.

Table 7: % Cumulative Drug Release (CDR) of batches E1 to E6

Time (min)	% Cumulative Drug Release					
	E1	**E2**	**E3**	**E4**	**E5**	**E6**
0	0	0	0	0	0	0
2	27.60	28.18	30.83	28.61	29.13	31.26
4	36.84	38.73	44.17	40.74	42.52	45.13
6	55.94	58.66	67.19	61.99	64.85	72.23
8	72.67	76.77	88.69	80.94	84.91	93.41
10	85.12	89.67	97.69	91.71	94.26	99.72

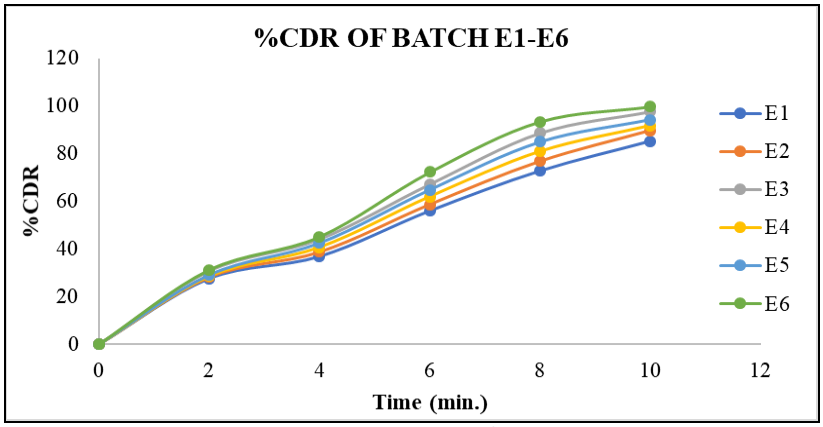

Figure 5: % Cdr Drug Release of Batches E1 – E6

RESULT OF STABILITY STUDY:

Based on the evaluation of various parameters, batch E6 was identified as the optimized batch as it demonstrated a 99.72 % drug release within 10 minutes, with a wetting time of 21.67 ± 1.53 seconds and an *in vitro* disintegration time of 24.67 ± 0.58 seconds, the shortest among all batches. Consequently, batch E6 was selected as the optimized batch. A stability study was conducted on the optimized batch at 40° ± 2 °C and 75 ± 5 % RH for one month. After this period, assessments of hardness, wetting time, *in vitro* disintegration time, and *in vitro* drug release were performed. The results, detailed in Tables 8 and 9, indicated no significant changes in these parameters, confirming the formulation's stability over time. A comparative study between the initial and post-stability results of the optimized batch is visually represented in Figure 6.

Table 8: Result of the Stability study

Sr. No.	Evaluation parameter	Results of optimized batch E6	Result after 1 month at 40° ± 2 °C and 75 ± 5 % RH
1	Hardness (kg/cme^2)	3.17 ± 0.58	3.33 ± 0.29
2	Wetting Time (sec.)	21.67 ± 1.53	23.33 ± 1.53
3	*in vitro* Disintegration Time (sec.)	24.67 ± 0.58	25.67 ± 0.58
4	Drug Content (%)	99.60 ± 0.26	99.07 ± 0.48

Table 9: *In vitro* Drug Release Study of Stability Batch

Time (Min.)	% CDR of Optimized Batch E6 (%)	% CDR of batch E6 After Time Period of 1 Month (%)
0	0	0
2	31.26	30.26

4	45.13	43.06
6	72.23	71.02
7	84.75	82.02
8	93.41	89.26
10	99.72	98.45

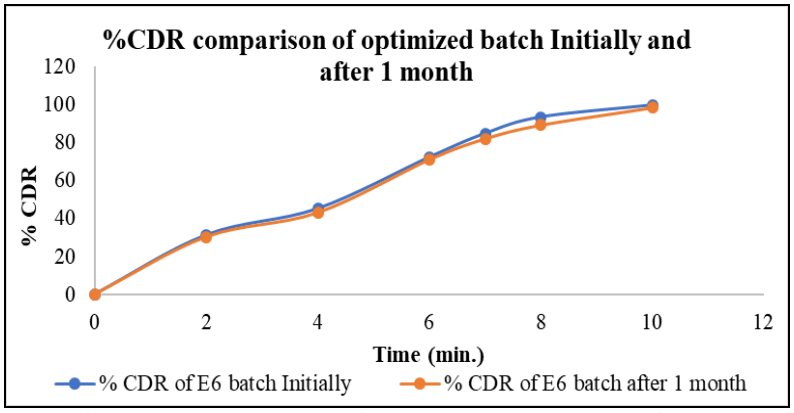

Figure 6: Comparison of *in vitro* Drug Release study of Optimized batch Initially and after 1 month of Stability study

The stability data indicated that all parameters remained within acceptable limits, with only minor changes in the results. Therefore, the prepared batch E6 was stable over a period of one month.

CONCLUSION:

The present study focused on the formulation and evaluation of sublingual tablets of eplerenone using natural disintegrants to enhance bioavailability and therapeutic performance. Due to its BCS class II nature and extensive first-pass metabolism, eplerenone exhibits limited oral bioavailability, necessitating an alternative delivery approach. The sublingual route was selected to bypass hepatic metabolism and achieve rapid onset of action.

Sublingual tablets were successfully prepared by direct compression using chitosan and karaya gum as natural disintegrants. Preformulation studies confirmed the identity and purity of the drug, while FTIR analysis indicated no significant drug–excipient interaction. All formulations demonstrated good flow properties and complied with pharmacopeial limits for post-compression parameters. Rapid wetting and disintegration were observed, supporting the suitability of natural disintegrants. Among all batches, formulation E6 showed optimal performance, with approximately 99.72% drug release within 10 minutes and the shortest disintegration time. Stability studies revealed no significant changes in key parameters, confirming formulation robustness. Overall, the developed sublingual tablet of eplerenone represents a promising strategy for improving bioavailability and achieving rapid therapeutic action in hypertension management.

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