

# Design, Development and Optimization of Buccal Tablet Containing Extract of *Terminalia chebula* Retz. for the Treatment of Asthma

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## ABSTRACT

**Objectives:** The aim of the study was to design, develop, and optimize the buccal tablets containing extract of *Terminalia chebula* Retz. for the treatment of asthma. **Materials and Methods:** Buccal tablets were made using the direct compression method, and screening tests with various polymers were run to see how they affected the properties of the tablets. The utilisation of response surface methods, two polymer types, carbopol® and HPMC, were chosen for additional optimization research. Strength of mucoadhesion and % two significant responses that the drug permeated after 8 hr from the buccal mucosa were chosen. By using a swelling index analysis, the profiles and kinetics of *in vitro* drug release were examined. **Results:** The *Terminalia chebula* Retz. content in buccal tablets was determined to be 99.14±0.44%, and a DSC analysis showed that there was no chemical interaction between the ingredients of the tablet (8 g carbopol 934 and 20 g HPMC K15 made up the optimal formulation). After 8 hr of *in vitro* dissolving studies, a cumulative *Terminalia chebula* Retz. release of 90% was reached, which was confirmed by swelling analysis. **Conclusion:** The findings suggested that *Terminalia chebula* Retz.'s. optimised buccal tablets would be a promising and different delivery method for the treatment of asthma.

**Keywords:** *Terminalia chebula* Retz., Buccal tablet, HPMC K15, Optimization, Carbopol, DoE.

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## INTRODUCTION

Despite the fact that oral drug delivery systems have many benefits, such as ease of ingestion and self-medication, the buccal route is the most effective at overcoming its drawbacks, such as the first-pass effect and enzymatic degradation.<sup>1</sup> Mucoadhesive nature helps to avoid possible drug metabolism by the liver and gastrointestinal route and instead directs blood flow into the jugular vein, increasing the bioavailability. The firm structure of the dose form causes some slight discomfort to the buccal cavity when using the buccal mucoadhesive method.<sup>2,3</sup>

One of the most significant indigenous multi-purpose tree species is *Terminalia chebula*, also known as Harar, Harra, Hirda, Myrobalan, and Haritaki. However, it is referred to as the "king of medications." "The species" fruits are used commercially in numerous Ayurvedic remedies to treat heartburn, flatulence,

dyspepsia, liver and spleen diseases, asthma, and constipation. They are also utilised locally in numerous medications and are a key component of "Triphala." There are numerous businesses, including Himalaya, Dabur, Organic India, Kapiva, Baidyanath, etc., that employ Harar to make their diverse goods. In addition to their medical and clinical applications, myrobalans are also employed in the manufacture of ink, as a mordant for basic aniline colours, and for tanning leather.<sup>4</sup> Wood is employed in the manufacturing of matchboxes, plywood, and building materials. It is also planted as a shade tree and used to make furniture, cabinets, and other interior fittings. Additionally, this plant serves as fodder. Fruit jam is used as a dietary supplement in various Indian states as well as in some gulf nations like Afghanistan and Pakistan. The tannin content in *Terminalia chebula* ranges from 27.3% to 40.0%, depending on the genotype and region.<sup>4</sup> Chebulic acid, chebulagic acid, corilagin, and gallic acid are the principal components of tannin. In addition to these, there are additional purgative anthraquinone and sennoside principles, amino acids, succinic acid, beta-sitosterol, resin, and amino acids. The leaves also have 2.75% calcium and 1.73% nitrogen, which is equivalent to 10.80% protein content. Additionally, it contains vitamins and minerals like Vitamin C. Protein, and amino acids.



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**Table 1: Layout of Two Factor Three-Level Design.<sup>9</sup>**

Independent Variables						
Factors	Coded Values			Actual Values in %		
X1	-1	0	+1	3	6	8
X2	-1	0	+1	20	24	28
Dependent Variables (Response)						
Y1- Mucoadhesive strength						
Y2- % Drug permeated after 8hr						

**Table 2: Composition of various buccal tablets prepared using 3<sup>2</sup> Full Factorial Design.**

Name of ingredients (mg)	NF1	NF2	NF3	NF4	NF5	NF6	NF7	NF8	NF9
<i>Terminalia chebula</i> Retz.	100	100	100	100	100	100	100	100	100
Carbopol 934	3	6	8	3	6	8	3	6	8
HPMC K15	20	20	20	24	24	24	28	28	28
Na-alginate	18	18	18	18	18	18	18	18	18
Sod. Saccharine	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Lactose	46.3	46.3	46.3	46.3	46.3	46.3	46.3	46.3	46.3
Talc	1	1	1	1	1	1	1	1	1
Mg-stearate	2	2	2	2	2	2	2	2	2

Additionally, there are some carbohydrates including glucose, sorbitol, fructose, and sucrose.<sup>5</sup>

## MATERIALS AND METHODS

### Collection of Plant Material

Fresh healthy *Terminalia chebula* Retz. leaves were collected from Rahuri Krishi Vidyapeeth and authenticated from the Botanical Survey of India, Pune (Voucher No- No.BSI/WRC/100-1/Tech/2022/41). The leaves were allowed to dry in shade under normal environmental condition for about one week and then crushed into small pieces by hand.<sup>6</sup>

### Materials

Alladin Industrial Corporation supplied Hydroxy Propyl Methyl Cellulose (HPMC). Chemdyes Corporation supplied Carbopol 934. (Ahmedabad, India). Loba Chemie Pvt. Ltd., supplied the Na-CMC and Na alginate (Mumbai, India). Finisar Chemical Ltd provided the Sod. Saccharine (Ahmedabad, India). SD Fine Chem. Ltd. supplied Ethyl Cellulose (EC) (Mumbai, India). Talc, lactose, PVP, Mg Stearate, ethanol, and acetonitrile were obtained from the SND College of Pharmacy, Yeola Chemicals Stores.

### Methods

#### Preparation of extract

*Terminalia chebula* Retz. leaves powder, 100 g in weight, was added to the Soxhlet extractor's thimble. Following the coupling

of the apparatus and connection of the condenser unit to an above-water tank to cool rising solvent vapours, 300 mL of the solvent (ethanol) was measured with a measuring cylinder and added to the still pot of the Soxhlet extractor. A Bunsen burner was used as the heat source, and it was set to 68°C.<sup>7</sup> The Soxhlet extractor's condenser unit is where the solvent condensed after evaporating through the distillation channel, thimble, and expansion adapter. The sample inside the thimble came into touch with the liquid droplets of the condensed vapour at this point. The whole contents of the thimble and syphon were poured back into the still pot of the Soxhlet extractor once the solvent in the thimble reached the level of the syphon top. In 3 hr, the procedure was repeated multiple times for nine refluxes, at which point the extraction was finished. The temperature was controlled by a thermometer.<sup>8</sup>

### Experimental Design

The design of the experiment was used for optimization of the Buccal tablet of *Terminalia chebula* Retz. A Full factorial experimental design of nine formulations was set up, using two factors at three levels.<sup>9</sup> The independent variables used were numeric factors namely, X1-concentration of Carbopol 934 and X2-concentration of HPMC K15. The responses selected for statistical optimization were, Y1- Mucoadhesive strength and Y2-% Drug permeated after 8hr showed in Table 1. Table 2 gives the composition of the *Terminalia chebula* Retz. buccal tablet.<sup>10</sup>

## The double direct compression method

The direct compression method was used to create the buccal mucoadhesive tablet. We employed excipients that were compatible with *Terminalia chebula* Retz. Everything was put through a sieve with a mesh size of 60. The necessary quantity was taken for the formulation, and a blender was used to fully combine it. To create the tablet, the combined powder was compressed using a compression device (Cadmach Machinery Co. Pvt. Ltd., India). The best formulation was created by direct compression in nine batches.<sup>11</sup>

## Evaluation of the pre-compressed powder

### Bulk Density

Accurately measure 2 g of granules that have been put into a graduated cylinder after passing through a 20# sieve. Level the powder gently without compacting it, then gauge the apparent volume of the unsettled mixture ( $V_0$ ). Use the following formula to determine the apparent bulk density in g/mL:<sup>8</sup>

$$\text{Bulk Density} = \frac{\text{Weight of powder}}{\text{Bulk volume}} \quad (1)$$

### Tapped Density

Weigh precisely 2 g of granules were put into a 10 mL graduated cylinder after passing through a 20# sieve. The sample container should then be mechanically tapped by being raised and let to fall under its own weight using a mechanically tapped density tester at a nominal rate of 100 drops. The tapped volume should then be measured to the closest graded units. Use the formula below to determine the tapped bulk density in g/mL.<sup>12</sup>

$$\text{Tapped Density} = \frac{\text{Weight of powder}}{\text{Tapped volume}} \quad (2)$$

### Compressibility (Carr's) index

To determine the initial bulk volume of each formula, pour a sample into a 10 mL graduated cylinder. The sample was then put under pressure by tapping until a consistent volume was reached.<sup>3</sup>

$$\text{Compressibility Index} = \frac{V_0 - V_t}{V_0} \times 100 \quad (3)$$

### Hausner's Ratio

An indicator of a powder or granular material's ability to flow is the Hausner's ratio.<sup>13</sup>

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \quad (4)$$

### Angle of repose

The powder mixture was poured into a fixed funnel and allowed to gently flow over a fixed diameter petri dish in order to calculate the angle of repose for each sample. The following equation was then used to get the angle of repose:<sup>13</sup>

$$\tan \theta = \frac{h}{r} \quad (5)$$

## Evaluation of the prepared buccal mucoadhesive tablets

### Weight variation

Twenty buccal tablets were weighed separately. The batch will be acceptable if no more than two tablets depart from the average weight by more than 7.5% and no tablets differ from the average weight by more than twice that amount.<sup>14</sup>

### Hardness test

The resistance and strength of the tablet to mechanical shocks is one of the most crucial factors while shipment and storage. YD-2 tablet hardness tester was used to determine the results of the hardness test (GUOMING). Six tablets were chosen at random from each formulation, and the mean and standard deviation values were computed.<sup>15</sup>

### Tablet friability

The friability was determined using a Roche-type friability. The number of tablets was precisely weighed in accordance with USP guidelines and placed in the tumbling device, which rotates at a speed of 25 rpm. In order to determine whether the percentage of loss was less than 1% or not, the tablets were dedusted, reweighed after 4 min, and then reweighed again.<sup>15</sup>

$$\text{Percentage Friability} = \frac{W_1 - W_2}{W_1} \times 100 \quad (6)$$

### Swelling index measurement

The buccal tablet was balanced perfectly and its weight was recorded while being placed on a glass slide. The tablet and cover slide were then placed in a Petri dish with 15 mL of phosphate buffer (a pH 6.8 solution that mimics the circumstances in the oral cavity). The tablet and cover slide were removed from the Petri dish at regular intervals for 6 hr, and any remaining surface water was carefully dried using filter paper. After swelling, the tablet was then reweighed ( $W_2$ ). The average was calculated after this experiment was conducted three times. The following equation describes how to measure the swelling index (water uptake).<sup>16</sup>

$$\text{Swelling Index} = \frac{W_1 - W_2}{W_1} \times 100 \quad (7)$$

### Content uniformity

This test is dependent on an analysis of the amount of the active ingredient in each tablet. In a glass mortar, 10 tablets of all formulations were ground into powder at random. A 10 mL conical flask with a stopper was filled with powder containing 1 mg of the medication. Acetonitrile was used to extract the medication, which was vigorously shaken before being filtered into a 10 mL volumetric flask. Utilizing phosphate buffer pH 6.8 to make known concentrations, additional acceptable dilutions

were made, and a UV-visible spectrophotometer was used to calculate absorbance at 387nm.<sup>16</sup>

### Mucoadhesive strength study

For evaluating mucoadhesion power, a well-known tool is the TA.XT plus texture analyzer. Instead of buccal mucosa, fresh sheep intestinal mucosal membrane was used. The mucosal membrane was able to come loose because the underlying loose connective tissues had been cut apart. The membrane remained washed with distilled water and then adjusted with a phosphate buffer pH 6.8 solution for 15 min. The tissue holder of the texture analyzer accessory was covered in and attached to a piece of the intestinal mucosa. The tissue membrane was then covered with a lid, and secured using thumbscrews, so that the lid's opening should only partially expose the tissue.<sup>17</sup> A magnetic stirrer was fastened to the accessory's base, and the temperature was raised to 37°C after the accessory was placed in a beaker of phosphate buffer with a pH of 6.8. Double-sided tape was used to secure the tablet to the probe. The accessory's aperture was positioned with the probe's tip just above the tissue membrane surface while the instrument arm was lowered. Before being withdrawn, the probe exerted 50 g of strain for 5 sec. After measuring it, the force required to remove the tablet from the membrane was multiplied by 0.0098. (Because the strength was recalibrated).<sup>18</sup>

$$\text{Mucoadhesive Force (N)} = \text{mucoadhesive strength(gm)} \times 0.0098 \quad (8)$$

### In vitro drug release

Using a USP type II dissolution test device (Paddle type), the release from the buccal mucoadhesive tablets from one side (unidirectional release) was investigated (Faithful, China). With addition to having an impermeable backing layer, as was previously mentioned, the buccal tablet was also wrapped in aluminium foil to ensure unidirectional release. It was then loaded in a dissolve device together with 500 cc of pH 6.8 phosphate buffers, spun at 50 rpm, and heated to 37°C. A spectrophotometer was used to analyse 5 mL samples obtained at intervals of up to

6 hr at 387 nm. Then, by plugging absorbance values into the equation for the calibration curve, it was possible to calculate the cumulative release of anastrozole from the manufactured tablets across different time frames.<sup>19</sup>

### Drug excipients compatibility study

To confirm the drug's compatibility with the primary, secondary polymers, and other additives in the selected formula, Differential Scanning Calorimetry (DSC) experiments and inspections were conducted. DSC is a remarkably sensitive method for determining how thermotropic a medication.<sup>20</sup>

## RESULTS

### Mucoadhesion study

All formulations performed mucoadhesion studies, and the results are displayed in (Table 3). The Design-Expert® Software was used to analyse the statistical experimental data. Table 3 displays the statistical design that resulted in 9 experimental runs.

### In vitro release study

A (type II) Dissolution apparatus was used to conduct an *in vitro* release study at pH 6.8, as mentioned in Figure 3.

### Drug-Excipients compatibility study

The medication's solubility was boosted by the peak's change from sharp to broad, and there is no interaction between the drug and the other ingredients, according to DSC spectra for the drug itself and its perfect formulation (Figures 4A and 4B).

## DISCUSSION

The prepared buccal tablet was subjected to various physicochemical evaluation of granules were represented in Table 4. Table 5 quantifies the physicochemical properties of the produced tablets. All of the tablets passed the USP weight variation test, and their hardness ranged from 4.32 to 8.4 to show that they had enough structural integrity forces to resist the storage and transportation circumstances.<sup>21</sup> In the tablets,

**Table 3: Mucoadhesive tablets with coded form and their responses.**

F. Code	Carbopol (Y1)	HPMC (Y2)	Mucoadhesive strength, Y1 (g)	% Drug permeated after 8 hr Y2 (%)
NF1	-1	-1	11.69±0.77	93.165±0.07
NF2	0	-1	23.07±0.26	91.042±0.29
NF3	1	-1	28.75±0.25	96.721±0.11
NF4	-1	0	14.53±0.55	87.776±0.35
NF5	0	0	22.25±0.91	82.997±0.14
NF6	1	0	33.52±0.36	80.046±0.62
NF7	-1	+1	18.62±0.31	83.198±0.13
NF8	0	+1	28.97±0.42	79.061±0.24
NF9	1	+1	37.87±0.58	67.145±0.41

Values are expressed in mean±SD (n=3).

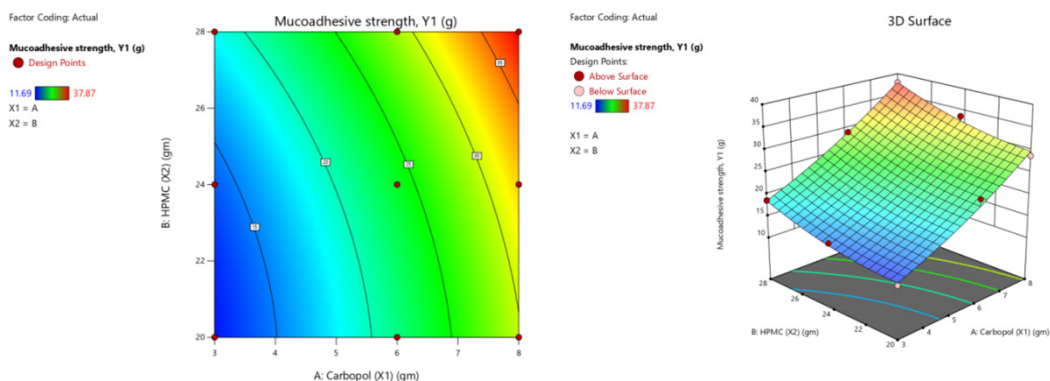


Figure 1: 2D and 3D response surface plot showing the effect of the amount of Carbopol 934 (X1) and HPMC K15 (X2) on Mucoadhesive Strength (Y1). (A) (B)

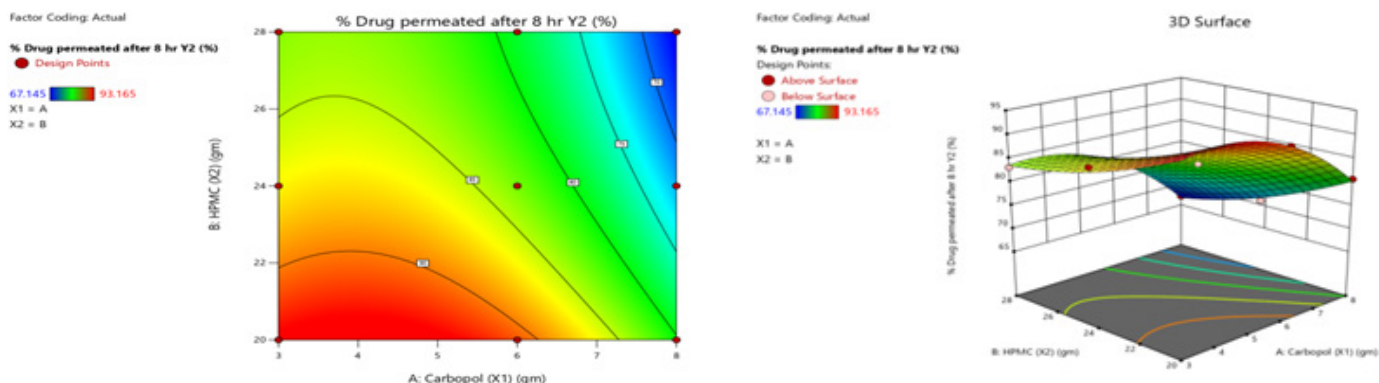


Figure 2: 2D and 3D response surface plot showing the effect of the amount of Carbopol (X1) and HPMC K15 (X2) on % Drug permeated after 8 hr (Y2).

we confirmed that this was the case. It was also noted that the hardness value increased as the principal mucoadhesive polymer content increased. The friability test results varied from 0.21 to 0.51 without any cracks, demonstrating that all formulations had remarkable mechanical resilience to any stress. Its surface pH values are between 5.5 and 7, which ensure that it won't cause any sensitization while in use and makes it suitable for the oral (salivary) pH. Figures 4 and 5 depict the DSC thermogram of *Terminalia chebula* Retz. and the physical combination of the formulation. The extract thermogram displayed an endothermic peak at 171.86°C, which is also its melting point. Peaks on the DSC thermogram for the formulation's extract-added physical mixture may be seen between 165.87°C and 170.93°C showed that there is no interaction between the excipients and the medication. Formulas comprising HPMC K15 and Carbopol 934 have quick hydration and swelling qualities (NF1 to NF9). The concentration of carbopol and HPMC K15 exhibits excellent mucoadhesion. There was less mucoadhesion as a secondary polymer due to the viscosity of the polymer, degree, and type of functional group substitution, generally speaking, to the non-ionic nature of HPMC K15, and there was a significant increase ( $p > 0.05$ ) in the mucoadhesion with the increase of Carbopol 934 concentration.<sup>22</sup>

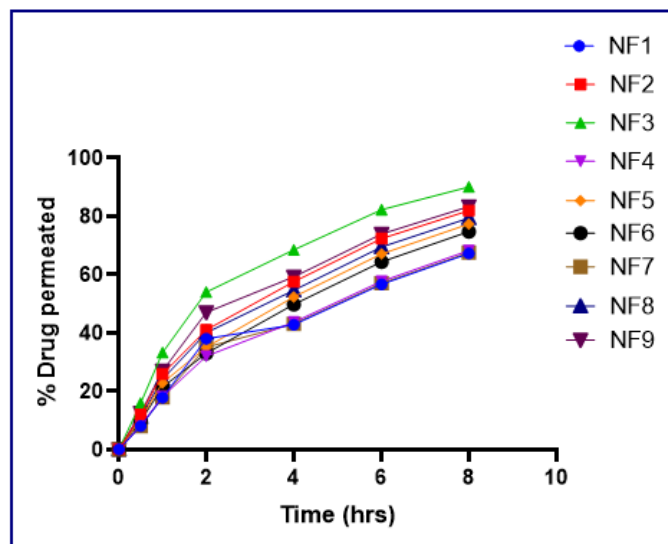


Figure 3: % Drug permeated from the formulations NF1 to NF9.

### Evaluation of powder blends of formulas

#### Evaluation tests of the formulated buccal tablets

*Terminalia chebula* Retz. mucoadhesive tablets have been optimized by RSM. HPMC K15 (%) and Carbopol 934 (%)

**Table 4: Results of Pre-compression parameters.**

F. Code	Bulk Density	Tapped Density	% Carr's Index	Hausner's Ratio	Angle of Repose
NF1	0.61±0.025	0.64±0.78	7.82±3.22	1.085±0.96	22.43±3.45
NF2	0.56±0.041	0.59±0.64	7.56±2.34	1.094±0.78	21.53±3.14
NF3	0.65±0.025	0.68±0.34	7.94±2.14	1.078±0.89	22.42±2.45
NF4	0.52±0.024	0.54±0.96	7.84±1.47	1.08±0.96	22.54±3.66
NF5	0.62±0.078	0.69±0.79	8.16±1.98	1.104±0.94	22.76±3.47
NF6	0.68±0.096	0.58±0.93	9.32±1.46	1.124±0.91	22.58±2.14
NF7	0.57±0.063	0.61±0.88	6.06±2.45	1.061±0.90	22.63±2.36
NF8	0.58±0.015	0.63±0.36	7.34±1.23	1.076±0.88	23.15±2.45
NF9	0.54±0.014	0.58±0.78	7.36±2.34	1.073±0.87	23.16±2.96

Values are expressed in mean±SD.

**Table 5: Physical features of tablets of *Terminalia chebula* Retz.**

F.Code	Hardness (kg/cm <sup>2</sup> )	Friability (%)	weight (mg)	Drug content (%)	Swelling Index	Surface pH	Mucoadhesion time
NF1	5.17±0.21	0.76±0.09	99.3±0.25	99.73±0.38	32.21±0.2	6.13± 0.05	7.25 hr
NF2	5.27±0.28	0.70± 0.10	99.1±0.18	98.94±0.37	34.87±0.1	6.26± 0.17	> 8 hr
NF3	5.43±0.23	0.68± 0.15	100.1±0.2	99.14±0.44	37.96±0.3	6.36± 0.15	> 8 hr
NF4	5.67±0.16	0.61±0.89	98.9±0.11	100.2±0.09	39.65±0.2	6.31± 0.23	7.5 hr
NF5	5.83±0.20	0.53±0.13	99.3±0.31	99.07±0.86	41.78±0.4	6.37± 0.10	> 8 hr
NF6	6.03±0.24	0.52±0.47	100.2±0.1	8.93±0.89	43.98±0.1	6.42± 0.17	> 8 hr
NF7	6.17±0.19	0.51±0.20	100.5±0.1	99.05±0.47	51.24±0.2	6.40±0.20	> 8 hr
NF8	6.28±0.17	0.50±0.86	99.2±0.26	99.97±0.07	54.04±0.1	6.66±0.13	> 8 hr
NF9	6.67±0.16	0.48± 0.05	98.9±0.21	98.33±0.75	56.25±0.3	6.58± 0.21	> 8 hr

Values are expressed in mean±SD (n=3).

were chosen as two numeric components based on the findings of polymer screening experiments, and restrictions were implemented to keep the overall polymer concentration between 20 and 28. Nine experiments using an optimal design with a quadratic model were carried out (Table 5). Y1: Mucoadhesive Strength, and Y2: % were identified as the critical response variables. Drug is absorbed 8 hr later. DoE and statistical analysis of the results were carried out utilising the Design-Expert® programme (Version. 13; Stat-Ease Inc., Minneapolis, MN, USA). The quadratic polynomials' equations 9 and 10 were used to forecast the outcome:

$$Y1 = +21.94 + 9.22*A + 3.63*B + 0.4704*AB + 1.30*A^2 + 1.39*B^2 \quad (9)$$

$$Y2 = +84.91 - 7.54*A - 5.86*B - 0.8973*AB - 5.59*A^2 + 1.78*B^2 \quad (10)$$

A and B denote the independent variables, and Y is the predicted response. Analysis of Variance (ANOVA) was used to determine how independent variables affected the replies, and

a *p*-value of 0.05 was used to determine whether the findings were statistically significant. Predicted and adjusted correlation coefficients (*R*<sup>2</sup>) were determined to assess the model's fitness. Three-dimensional (3D) surface graphs were used to depict the experimental design region and track independent variables' influence on the outcomes. The obtained experimental results were compared with the predicted values after the improved formulation had been developed. ANOVA was used to examine the regression models shown in Table 6 for Y1 and Table 7 for Y2. In the instance of Y1, the model equation's high *F* value (46.52) and low *p*-value (0.0048) show that it was statistically significant. The 2D and 3D plot for mucoadhesive strength (Y1) shown in Figure 1.<sup>23</sup> The *R*<sup>2</sup> score of 0.9873, which showed that this model can account for 98.73% of the response's variability, confirmed the regression model's degree of confidence. High correlation between expected and observed values was shown by the close agreement between the predicted *R*<sup>2</sup> value of 0.8948 and the adjusted *R*<sup>2</sup> value of 0.9660. For Y2, the importance of the model equation was implied by the high model *F* value (166.04) and low *p*-value (0.0007). The 2D and 3D plots for drug permeated after

**Table 6: ANOVA of Quadratic models for Y1.**

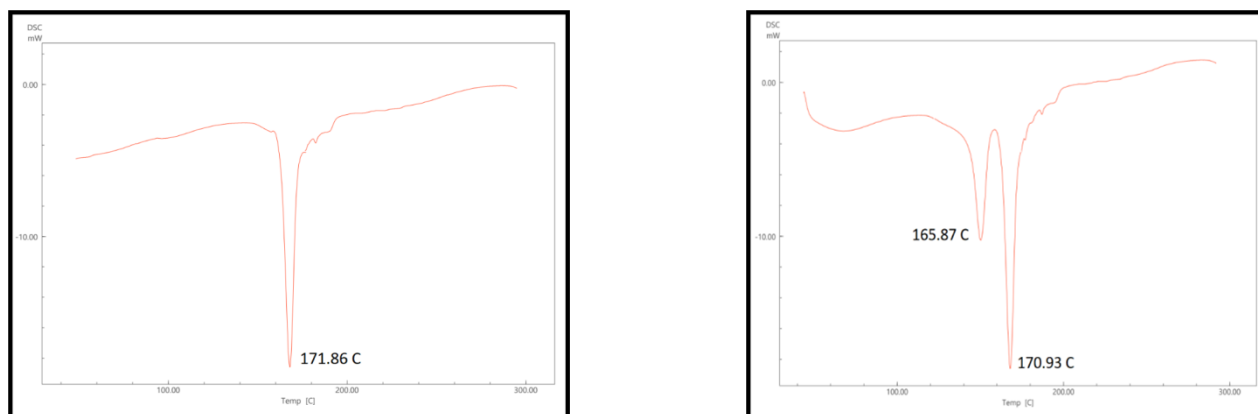
Source	Sum of Squares	d <sub>f</sub>	Mean Square	F-value	p-value	Significant
Model	595.49	5	119.1	46.52	0.0048	
A-Carbopol (X1)	509.68	1	509.68	199.08	0.0008	
B-HPMC (X2)	78.41	1	78.41	30.63	0.0116	
AB	0.8969	1	0.8969	0.3503	0.5956	
A <sup>2</sup>	3.05	1	3.05	1.19	0.3548	
B <sup>2</sup>	3.89	1	3.89	1.52	0.3054	
Residual	7.68	3	2.56			
Cor Total	603.17	8				

Note: R<sup>2</sup> = 0.9873, Adjusted R<sup>2</sup> = 0.9660, Predicted R<sup>2</sup> =0.8948. Abbreviation: ANOVA: Analysis of Variance.

**Table 7: ANOVA of Quadratic models for Y2 (Type III – Partial).**

Source	Sum of Squares	d <sub>f</sub>	Mean Square	F-value	p-value	significant
Model	590.63	5	118.13	166.04	0.0007	
A-Carbopol (X1)	340.91	1	340.91	479.21	0.0002	
B-HPMC (X2)	204.75	1	204.75	287.81	0.0004	
AB	3.26	1	3.26	4.59	0.1217	
A <sup>2</sup>	56.82	1	56.82	79.88	0.003	
B <sup>2</sup>	6.35	1	6.35	8.93	0.0582	
Residual	2.13	3	0.7114			
Cor Total	592.76	8				

Note: R<sup>2</sup> = 0.9873, Adjusted R<sup>2</sup> = 0.9660, Predicted R<sup>2</sup> =0.8948. Abbreviation: ANOVA: Analysis of Variance.



**Figure 4:** DSC of extract *Terminalia Chebula* Retz. (A) and DSC of extract + Excipients (B).

8hr (Y2) are shown in Figure 2. With an R<sup>2</sup> score of 0.9964, the model was able to account for 99.64% of the response's variability. Additionally, there was a strong correlation between the adjusted R<sup>2</sup> (=0.9904) and the projected R<sup>2</sup> (=0.9524), demonstrating the model's high level of prediction.

**ANOVA of models for Mucoadhesive Strength (Y1)**

**ANOVA of models for % Drug permeated after 8 hr (Y2)**

The design study's outcomes were used to identify the ideal formulation composition. Design objectives were maximised

(Y1) and maximised (Y2). The mucoadhesion of the buccal tablets was really improved by the combination of the two polymers. The HPMC K15 highly cross-linked structure offers a broad surface area for the best possible interaction with the mucosa.

The optimised formulation's coded variables were discovered to be A=8 and B=20 (NF3). A new optimised formulation was created in order to assess the model's accuracy under ideal circumstances. The content of *Terminalia chebula* Retz. in buccal tablets was determined to be 99.14±0.44%, ensuring consistent dosage. The powder mixture and buccal tablet physical characterisation experiments for the improved formulation are

summarised in Table 5. The model's importance and validity were demonstrated by the close agreement between the observed experimental values and the anticipated values (RSD, 2%). The *in vitro* dissolution patterns of *Terminalia chebula* Retz. and free drug as a control are shown in Figure 3. In the first half hour, a cumulative *Terminalia chebula* Retz. release of  $15.89 \pm 3.05\%$  was seen, indicating a modest burst release from buccal tablets. Following that, a consistent drug release was noticed over the following 8 hr, achieving a cumulative release of  $90.04 \pm 4.71\%$ .

## CONCLUSION

The controlled release RSM studies were employed to successfully design and optimise buccal tablets of *Terminalia chebula* Retz. for the use of HPMC K15 and carbopol 934 as mucoadhesive polymers. The improved formulation's powder mixture demonstrated adequate flow, and the buccal tablets' physical and mucoadhesive qualities were adequate. The properties of the improved formulation closely matched the values predicted by the design model. Buccal pills swelled quickly, and over the course of 8 hr, a controlled drug release was accomplished. In order to treat asthma, it was determined that buccal tablets would be used as an alternative method of delivery. For controlled drug release of *Terminalia chebula* Retz., these tablets were designed, evaluated, and optimised.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**FTIR:** Fourier Transform Infrared spectroscopy; **DSC:** Differential scanning calorimetry; **HPMC:** Hydroxypropyl methylcellulose; **EC:** Ethyl cellulose; **UV:** Visible Spectrophotometer; **USP:** United States Pharmacopoeia; **RPM:** Revolutions per minute.

## SUMMARY

This research was done to design, develop, and optimise a buccal tablet containing an extract of *Terminalia chebula* Retz. for the treatment of asthma that has the highest bioavailability and gets the drug to the buccal mucosa without going through the liver first. The examination of some mucoadhesive polymers from naturally occurring edible sources is a further study. Due to its special capacity to disguise bitter tastes, the dosage form created is anticipated to have higher patient acceptability. These dosage forms also have the meritorious benefits of being biodegradable and biocompatible. For the preparation of buccal tablets for *Terminalia chebula* Retz., various polymers including HPMC K15 and carbopol 934 in combination with different concentrations have been used. Additionally, an evaluation of the powder flow properties for buccal tablets, including the angle of

repose, bulk density, tapped density, Hausner's ratio, and Carr's compressibility index, was performed. The prepared buccal tablets were evaluated for quality control tests, including consistency of weight, thickness, hardness, friability, disintegration time, and drug content. Other tests include those for *in vitro* drug release, surface pH, swelling index, and mucoadhesive strength.

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