RESEARCH PAPER

Formulation Design and Evaluation of Sublingual Tablets of Buspirone HCL

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ABSTRACT

The present study was undertaken to formulate and optimize sublingual tablets of Buspirone HCl for rapid onset of action in the management of anxiety disorders. Buspirone HCl exhibits low oral bioavailability due to extensive first-pass metabolism, necessitating an alternative delivery approach. Sublingual tablets were prepared by direct compression using superdisintegrants such as Glycolys and Solutab. Preformulation studies confirmed drug identity with a melting point of 198–202 °C. A calibration curve showed excellent linearity with R^2 = 0.998. The formulations were evaluated for pre-compression parameters and post-compression parameters including hardness, friability, and drug content, wetting time, while disintegration time was 14.33–29.23 seconds. A 3^2 factorial design optimized the formulation, and batch BS9 exhibited rapid disintegration and maximum drug release (99.36% within 12 minutes). Stability studies confirmed no significant changes under accelerated conditions. Thus, the optimized sublingual tablets demonstrated improved dissolution, rapid onset, and potential for enhanced therapeutic efficacy and patient compliance.

Keywords: Buspirone HCl, Sublingual tablets, Superdisintegrants, Factorial design.

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INTRODUCTION

Anxiety is an integral human emotion that serves as a protective mechanism, enabling individuals to respond effectively to potential threats or stress. However, when anxiety becomes excessive, persistent, and disproportionate to actual circumstances, it evolves into a pathological condition known as an anxiety disorder. Among the spectrum of anxiety disorders recognized in clinical practice, Generalized Anxiety Disorder (GAD) represents one of the most prevalent and functionally debilitating conditions, characterized by chronic, excessive worry, restlessness, and physiological symptoms such as muscle tension, palpitations, and sleep disturbances. The disease typically manifests insidiously and tends to persist over several years, affecting an individual's emotional well-being, occupational functioning, and quality of life.

Pharmaceutical and clinical research over the past two decades has established that anxiety disorders are neurobiological in origin**,** involving complex interactions between neurotransmitter systems, particularly serotonin, dopamine, norepinephrine, and gamma-aminobutyric acid (GABA). Dysregulation within these systems leads to heightened neuronal excitability and persistent anxiety states. GAD differs from transient anxiety in that it is not situation-specific but rather a continuous and pervasive state of apprehension. The disorder often coexists with depressive episodes, substance use disorders, and other psychosomatic conditions, adding further complexity to its management.[1-4]

MATERIALS AND METHODS

Materials:

Avicel PH 102, Mannitol, Sodium lauryl sulfate, Aspartame, Magnesium stearate, and talc were procured from Chemdyes, Rajkot, Gujarat, India.

Fabrication of Sublingual Tablets

Sublingual tablets were prepared by the direct compression method. All ingredients were passed

through sieve no. 60 and blended uniformly using geometric dilution. The prepared powder blends were compressed using a rotary tablet compression machine with flat-faced punches. The tablet weight was kept constant for all formulations. [5-7] (Table 1 and 2).

Table 1: Formulation batches of Buspirone HCl sublingual tablet

Ingredients (mg)	B	B	B	B	B	B	B	B	B
Buspirone HCl	5	5	5	5	5	5	5	5	5
Avicel pH 102	3	3	3	3	3	3	3	3	3
Glycolys	2	3	4	2	3	4	2	3	4
Solutab	2	2	2	3	3	3	4	4	4
D-mannitol	7	7	7	7	7	7	7	7	6
Aspartame	2.	2.	2.	2.	2.	2.	2.	2.	2.
SLS	1.	1.	1.	1.	1.	1.	1.	1.	1.
Talc	2.	2.	2.	2.	2.	2.	2.	2.	2.
Magnesium stearate	1.	1.	1.	1.	1.	1.	1.	1.	1.
Total weight	1	1	1	1	1	1	1	1	1

3^2 FACTORIAL DESIGN

- A 3^2 factorial design was applied to evaluate combined effect of Glycolys and Solutab.
- In this design 2 dependent variables were selected, where each variable was evaluated at three different levels –1, 0 and +1.
- This design is suitable for exploration of quadratic response and the second order polynomial model; thus, it helps in the optimization through small number of experimental runs.
- In 3^2 factorial design amount of Glycolys was taken as independent variable X_1 where amount of Solutab was taken as independent variable X_2 and *In Vitro* Disintegration time and % cumulative drug release at 12 mins. were selected as a dependent variable.
- Data of response (dependent variables) was recorded and analysis of data was carried out using ANOVA in the design expert 13 trial version provided by stat ease.
- The Quadratic equation for 3^2 factorial design is as follows:

$$Y = B_0 + B_1X_1 + B_2X_2 + B_{12}X_1X_2 + B_1^2X_1^2 + B_2^2X_2^2 + E$$

Where,

B_0	=	Intercept Constant
B_1 and B_2	=	Coefficient of X_1 and X_2 coefficient of first order term
B_{12}	=	Coefficient of interaction between X_1 and X_2 variable
B_{11} and B_{22}	=	Coefficient of Quadratic term
X_1 and X_2	=	Independent variable
E	=	Error

Table 2: Coded and Actual value of formulations

Run	Coded value		Actual value	
	(Glycolys)	(Solutab)	Amount of Glycolys (mg)	Amount of Solutab (mg)
1	-1	-1	2	2
2	0	-1	3	2
3	+1	-1	4	2
4	-1	0	2	3
5	0	0	3	3
6	+1	0	4	3
7	-1	+1	2	4
8	0	+1	3	4
9	+1	+1	4	4

Determination of precompression parameters

Hausner's ratio, bulk density, tapered density, compressibility index, and angle of repose were all measured. Good flow qualities were indicated by the powder mixture's minimum Carr's index, Hausner's ratio, and angle of repose.

Bulk density: Carefully weigh the powder mixture and transfer it to a measuring cylinder. Measure the volume of the powder without applying pressure. The volume is expressed as grams per milliliter (gm/ml). [8-10]

Tapped density: The tapped density was determined by placing a graduated cylinder containing the formulation blend on a mechanical tapping apparatus. The volume was tapped until a constant tapped volume was achieved. Tapped density is expressed as grams per milliliter (gm/ml). [8-10]

Hausner's ratio: Hausner's ratio, determined by dividing the tapped density by the bulk density of a powder, serves as an indicator of powder flow. A ratio at or below 1.25 signifies favorable flow properties, while a ratio surpassing 1.25 indicates inadequate flow. [8-10]

Compressibility index: The compressibility index is a percentage value obtained by calculating the difference between the tapped density and bulk density of a material, then dividing this difference by the tapped density. It serves as a measure of the compressibility or ability of a powder to decrease in volume under pressure. [8-12]

Angle of repose: Angle of repose was determined by funnel method. Powder blend was poured from funnel that can be raised vertically until it reaches maximum cone height (h) was obtained. Radius (r) of the pile was measured. Angle of repose was measured by following formula. [8-12]

$$\mathbf{Tan\ \theta = \frac{h}{r}}$$

$$\mathbf{\theta = \tan^{-1}\frac{h}{r}}$$

Where, θ = Angle of repose, h = Height of pile, r = Radius of pile

Determination of post compression parameters

Thickness and diameter: Tablet thickness and diameter were determined using Digimatic Vernier calipers. 6 tablets were chosen, and their thickness and diameter were measured by positioning them between the 2 arms of the Vernier calipers. [13-16]

Hardness: Tablet hardness refers to the force necessary to fracture a tablet in a diametric compression trial. The crushing strength of tablets was assessed using a Monsanto-type hardness tester. [13-16]

Weight variation: Twenty tablets were randomly selected, and their collective weight was determined using an electronic balance to establish an average weight. [13-16]

Friability test: The friability of the tablets was assessed using a Roche-type friabilator. Initially, twenty tablets were weighed, then subjected to the friabilator's rotation at 25 rpm for 4 minutes. Afterward, the tablets were removed and weighed again. The acceptable loss in weight should not exceed 1%. The percentage friability was calculated using the provided equation. [17-19]

$$\mathbf{\%\ Friability = \frac{Initial\ weight - Final\ w}{Initial\ weight}}$$

Drug content: 10 tablets were pulverized, and an amount equivalent to 5 mg of Buspirone HCl was weighed and dissolved in 100 ml of phosphate buffer with a pH of 6.8. After filtration, 2 ml of the filtrate was diluted to 10 ml, and the absorbance of this solution was assessed using a UV spectrophotometer at a wavelength of 244 nm. [17-19]

***In Vitro* Disintegration test:** The test involved using a digital tablet disintegration test apparatus to assess six tablets. Phosphate buffer with a pH of 6.8, maintained at a temperature of 37 ± 0.5 °C, served as the disintegration media. The time taken, measured in seconds, was recorded for the tablets to completely disintegrate, leaving no residue in the apparatus. [20-22]

***In Vitro* Drug release study:** The % of drug release from Buspirone HCl sublingual tablets was assessed using the USP type II dissolution apparatus, operating at 50 rpm and maintained at 37° ± 0.5°C with 900 ml of phosphate buffer (pH 6.8). Samples were withdrawn at regular intervals, replaced with fresh dissolution media, and filtered through a 0.45µm membrane filter. The absorbance of these samples was analyzed using a UV at a wavelength of 244 nm. [20-22]

Stability study of optimized batch: 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 aluminium foil to prevent the formulation from exposure to light under the 40° ± 2 °C / 75 ± 5% RH for 1 month as prescribed by ICH guidelines for accelerated stability study. After completion of 30 days tablets were evaluated for Hardness, Friability, Drug content, Wetting time, In Vitro Disintegration time and In Vitro Drug Release study.

RESULTS AND DISCUSSION

Identification of drug

Melting point Melting point determination, a commonly employed technique for drug identification, was conducted using a melting point apparatus, revealing a range of 198 - 202 °C for Buspirone HCl. This falls within the reported melting point range of 201.5 – 202.5 ℃ for Buspirone HCl. Consequently, it was inferred that the provided substance is indeed Buspirone HCl.

Estimation of Buspirone HCl by UV-Visible Spectrophotometry

A standard stock solution of Buspirone HCl was made by dissolving 10 mg of Buspirone HCl in 100 ml of phosphate buffer (pH 6.8), resulting in a stock solution with a concentration of 100 µg/ml. To determine the λmax, the stock solution was scanned from 200 to 400 nm using a UV-Visible spectrophotometer, with phosphate buffer (pH 6.8) used as the blank. Working solutions of concentrations ranging from 2 to 10 ppm were prepared by pipetting 0.2, 0.4, 0.6, 0.8, and 1 ml, respectively, from the stock solution of 100 ppm and diluting each up to 10 ml in a volumetric flask. The absorbance of these working solutions was measured in triplicate at a wavelength of 244 nm against phosphate buffer (pH 6.8) as the blank (Figure 1,2 and Table 3)

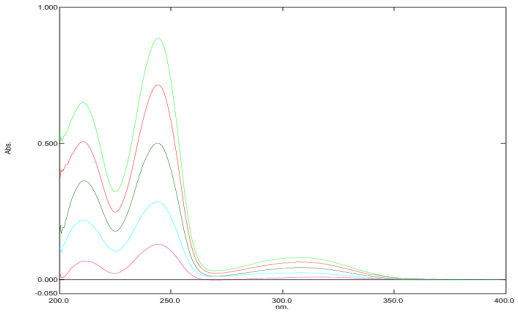

Fig. 1: Overlay Spectra of Buspirone HCl in phosphate buffer pH 6.8

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

Sr.	Concentration (ppm)	Absorbance			Mean Absorbance ± S.D.
		I	II	III	
1	2	0.122	0.119	0.123	0.121 ± 0.0021
2	4	0.289	0.286	0.285	0.287 ± 0.0021
3	6	0.506	0.502	0.501	0.503 ± 0.0026
4	8	0.716	0.718	0.715	0.716 ± 0.0015
5	10	0.894	0.892	0.894	0.893 ± 0.001
					2

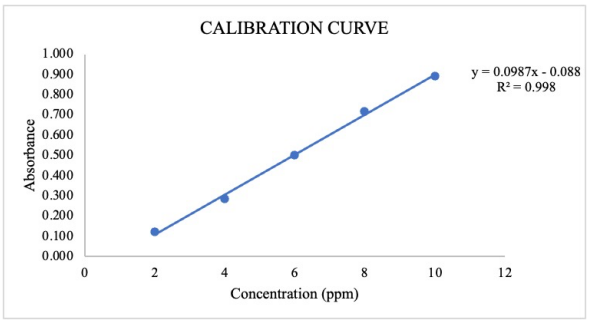

Fig. 2: Calibration curve of Buspirone HCl in phosphate buffer at pH 6.8

Precompression Parameters

The powder blend's bulk density, taped density, Hausner's ratio, Carr's index, and angle of repose were all measured. It was discovered that every parameter had acceptable flow characteristics. The bulk density values ranged from 0.54 ± 0.01 to 0.88 ± 0.02 g/ml, while the tapped density varied between 0.56 ± 0.00 and 1.09 ± 0.05 g/ml, indicating satisfactory packing characteristics of the powder blends.

The Hausner's ratio values were found to be between 1.04 ± 0.01 and 1.23 ± 0.08. Batches BS3, BS4, BS5, BS6, BS7, and BS8 exhibited Hausner's ratio values close to 1.10, suggesting good flow properties, whereas batches BS1 and BS2 showed slightly higher values (1.23 ± 0.08), indicating passable flow behaviour.

The Carr's index values ranged from 3.56 ± 1.20% to 18.76 ± 4.99%. Lower Carr's index values observed for batches BS3 and BS4 indicated excellent compressibility, while moderate values for other batches suggested acceptable compressibility. The angle of repose for all formulations was below 30°, ranging from 27.35 ± 0.35° to 29.51 ± 0.40°, confirming satisfactory flow characteristics. Overall, the low standard deviation values indicated uniformity and reproducibility of the blends, and all factorial design batches were found to possess suitable pre-compression properties for tablet formulation. (Table 4).

Table 4: Precompression Parameters

tch	Bulk density gm/ml)	Tapped density gm/ml)	Hausner's Ratio	Carr's index (%)	ngle of repose (°θ)
S1	8 ± 0.02	09 ± 0.05	1.23 ± 0.	18.76 ± 4.9	29.51 ± 0.4

			08	9	0
S2	8 ± 0.02	09 ± 0.05	1.23 ± 0.08	18.76 ± 4.99	28.85 ± 1.01
S3	4 ± 0.01	56 ± 0.00	1.04 ± 0.01	3.56 ± 1.20	27.35 ± 0.35
S4	5 ± 0.02	93 ± 0.03	1.09 ± 0.02	7.97 ± 2.06	28.83 ± 0.38
S5	5 ± 0.02	93 ± 0.03	1.09 ± 0.02	7.97 ± 2.06	28.83 ± 0.38
S6	5 ± 0.02	95 ± 0.02	1.11 ± 0.04	10.19 ± 3.22	28.83 ± 0.38
S7	5 ± 0.02	94 ± 0.02	1.10 ± 0.02	9.08 ± 1.90	28.61 ± 0.38
S8	5 ± 0.02	94 ± 0.02	1.10 ± 0.02	9.08 ± 1.90	28.61 ± 0.38
S9	4 ± 0.02	98 ± 0.04	1.16 ± 0.07	13.41 ± 5.64	28.18 ± 0.37

Physical characteristics such as thickness, diameter, weight variation, hardness and friability were measured. The tablet thickness across all batches was found to be uniform, ranging from 3.13 ± 0.35 mm to 3.43 ± 0.31 mm, indicating consistent die filling and compression during tableting. The weight variation values ranged between 119.50 ± 0.89 mg and 120.30 ± 1.49 mg, and all formulations complied with pharmacopoeial limits, confirming uniform granule flow and proper mixing. The hardness of the tablets was observed to be in the range of 2.17 ± 0.29 to 3.33 ± 0.58 kg/cm², suggesting adequate mechanical strength to withstand handling without adversely affecting disintegration and drug release. Slight variations in hardness among the batches may be attributed to differences in superdisintegrant concentration and granule bonding. The friability values for all formulations were below 1%, ranging from 0.55% to 0.76%, indicating good resistance to abrasion and mechanical stress. Overall, the low standard deviation values across all parameters demonstrated uniformity and reproducibility of the tablet batches. The results confirmed that all factorial design formulations possessed acceptable post-compression characteristics and were suitable for further *In-vitro* evaluation and optimization studies. (Table 5).

The wetting time values ranged from 12.19 ± 0.12 s to 27.28 ± 0.99 s, indicating rapid penetration of the dissolution medium into the tablet matrix. A progressive reduction in wetting time was observed from BS1 to BS9, suggesting improved wicking and swelling efficiency with optimized superdisintegrant combinations. Batch BS9 exhibited the lowest wetting time, reflecting enhanced water uptake capacity. The *In-vitro* disintegration time ranged between 14.33 ± 0.58 s and 29.23 ± 1.11 s. Formulations containing higher and optimized levels of superdisintegrants (BS7–BS9) showed significantly faster disintegration, whereas BS1–BS3 exhibited comparatively longer disintegration times. This trend confirms the synergistic effect of Glycolys and Solutab in promoting rapid tablet breakup. The drug content of all batches was found to be within acceptable limits, ranging from 98.72 ± 0.43% to 99.13 ± 0.59%, indicating uniform drug distribution and reproducibility of the formulation process. Overall, the results demonstrated that factorial design batches possessed excellent wetting, rapid disintegration, and consistent drug content, making them suitable for further dissolution and optimization studies. (Table 6).

Post compression parameters

Table 5: Post compression parameters of Buspirone HCl Sublingual tablets

Batch	Thickness (mm ± S.D.)	Weight variation (mg ± S.D.)	Hardness (kg/cm² ± S.D.)	Friability (%)
BS1	3.27 ± 0.21	119.60 ± 1.14	3.33 ± 0.58	0.55
BS2	3.43 ± 0.31	120.20 ± 1.24	3.17 ± 0.76	0.61
BS3	3.37 ± 0.15	120.30 ± 1.49	2.83 ± 0.29	0.63
BS4	3.33 ± 0.06	120.05 ± 0.83	3.17 ± 0.29	0.58
BS5	3.27 ± 0.49	119.65 ± 1.18	2.83 ± 0.29	0.67
BS6	3.40 ± 0.17	119.60 ± 1.43	2.50 ± 0.87	0.68
BS7	3.13 ± 0.35	119.50 ± 0.89	2.50 ± 0.50	0.71
BS8	3.37 ± 0.42	120.30 ± 1.45	2.33 ± 0.58	0.74
BS9	3.33 ± 0.38	119.60 ± 1.43	2.17 ± 0.29	0.76

Table 6: Wetting time, *In Vitro* disintegration time and Drug Content

Batch	Wetting time (sec. ± S.D.)	*In-vitro* disintegration time (sec. ± S.D.)	Drug content (%)
BS1	27.28 ± 0.99	29.23 ± 1.11	99.08 ± 0.22
BS2	22.88 ± 0.55	24.14 ± 0.73	98.72 ± 0.43
BS3	21.25 ± 0.96	23.79 ± 0.88	98.79 ± 0.43
BS4	26.60 ± 1.08	25.06 ± 0.74	98.91 ± 0.67
BS5	16.53 ± 0.47	19.06 ± 0.50	98.98 ± 0.64
BS6	16.13 ± 0.59	18.29 ± 0.76	99.05 ± 0.60
BS7	15.75 ± 0.68	17.04 ± 0.66	99.04 ± 0.74
BS8	14.44 ± 0.13	16.21 ± 0.16	99.13 ± 0.47
BS9	12.19 ± 0.12	14.33 ± 0.58	99.13 ± 0.59

In Vitro Drug Release study

The *In-vitro* dissolution study of factorial design batches BS1–BS9 was carried out to evaluate the effect of combined superdisintegrants on the % cumulative drug release (% CDR). All formulations exhibited a rapid initial drug release, with 45.85–58.26% CDR within 2 minutes, indicating efficient tablet wetting and quick onset of disintegration. This was followed by a progressive increase in drug release with time. Batches BS1–BS3 showed comparatively slower release profiles, achieving around 95–98% drug release by 16–18 minutes, which may be attributed to lower levels of superdisintegrant combination. In contrast, batches BS6–BS9 demonstrated faster and more complete drug release, reaching above 98% CDR within 12–14 minutes, reflecting the synergistic effect of Glycolys and Solutab on tablet disintegration and drug diffusion. Among all formulations, batch BS9 exhibited the most rapid and complete drug release, achieving 99.64% CDR at 14 minutes, indicating optimal superdisintegrant concentration. The dissolution profiles of all batches were smooth and reproducible, as supported by the graphical representation. Overall, the results confirmed that the combination of Glycolys and Solutab significantly enhanced the dissolution performance, and the factorial design approach effectively optimized the formulation for rapid drug release. (Table 7 and Figure 3).

Table 7: Percentage Cumulative drug release of batches BS1 to BS9

Ti (M	B	B	B	BS	B	B	B	B	B
0	0	0	0	0	0	0	0	0	0
2	45	48	49	46.	50	54	52	56	58
4	58	64	65	62.	65	67	66	68	69
6	66	70	74	70.	75	78	78	80	81
8	76	79	84	78.	85	89	88	91	92
10	78	80	81	78.	89	93	92	94	97
12	81	84	89	82.	90	95	94	96	99
14	86	91	95	87.	96	99	98	99	-
16	95	98	98	96.	99	-	-	-	-
18	98	-	-	99.	-	-	-	-	-

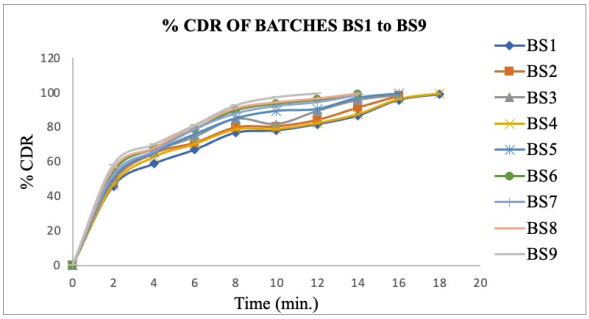

Fig. 3: In-vitro drug release of Batches BS1 to BS9

STATISTICAL ANALYSIS

- A statistical model incorporating polynomial and interactive terms is used to evaluate the response

$$Y = B_0 + B_1X_1 + B_2X_2 + B_{12}X_1X_2 + B_{11}X_1^2 + B_{22}X_2^2 + E$$

- The values of dependent variables and results of ANOVA analysis are displayed in below tables 8,9 and 10.

Table 8: Observed Dependent Variables for 3^2 Factorial Design

Batch code	*In-vitro* disintegration time (sec. ± S. D.)	% CDR at 12 min.
BS1	29.23	81.55
BS2	24.14	84.05
BS3	23.79	89.32
BS4	25.06	82.35
BS5	19.06	90.47
BS7	18.29	95.82
BS6	17.04	94.56
BS8	16.21	96.73
BS9	14.33	99.36

Table 9: Summary of ANOVA Analysis

Source	Sum of Square	Degree of Freedom	Mean Square	F Value	P Value
***In-vitro* Disintegration time (Y_1)**					
Regression	189.18	5	37.84	17.45	0.0200
Residual	6.50	3	2.17	-	-
Total	195.69	8	-	-	-
% CDR at 12 min (Y_2)					
Regression	331.80	5	66.36	10.05	0.0431
Residual	19.81	3	6.60	-	-
Total	351.61	8	-	-	-

Table 10: Summary of Polynomial Equation

Response	B_0	B_1	B_2	B_{12}	B_1^2	B_2^2
***In-vitro* Disintegration Time (Y_1)**						
Coefficient	+19.81	-2.49	-4.93	+0.6843	+1.49	-0.0141
P Value (Glycolys)	0.0256					
P Value (Solutab)	0.0038					
% CDR at 12 min (Y_2)						
Coefficient	+89.5	+4.3	+5.9	-0	+0.076	+1.38
t	0	4	5	.7425	7	
P Value (Glycolys)	0.0256					
P Value (Solutab)	0.0108					

Statistical Analysis for *In-vitro* Disintegration Time

- The quadratic model developed for *In-vitro* disintegration time was found to be statistically significant, as indicated by a significant model F-value and p-value (< 0.05). Both formulation variables, Glycolys (B1) and Solutab (B2), showed a pronounced influence on the response.

$$Y_1 = 19.81 - 2.49B_1 - 4.93B_2 + 0.6843B_1B_2 + 1.49B_1^2 - 0.0141B_2^2$$

The polynomial equation reveals that the negative coefficients of B_1 and B_2 indicate that increasing concentrations of Glycolys and Solutab significantly reduce the disintegration time, with Solutab exhibiting a stronger effect.

- The positive interaction term (B_1B_2) suggests a synergistic effect between the two superdisintegrants. The quadratic terms indicate curvature in the response, confirming the suitability of a quadratic model.
- The ANOVA findings confirm the statistical significance of the developed model, as evidenced by a p-value below 0.05. Both primary formulation factors exerted a significant effect on the *In-vitro* disintegration time. The high coefficient of determination ($R^2 > 0.94$), along with a satisfactory adjusted R^2 value, demonstrates good model fit and supports the reliability of the model for predictive purposes. (Fig 4,5 and 6)

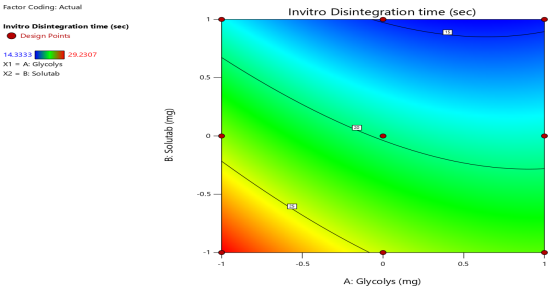

Fig. 4: Contour plot showing the effect of Glycolys (X_1) and Solutab (X_2) on *In-vitro* Disintegration time

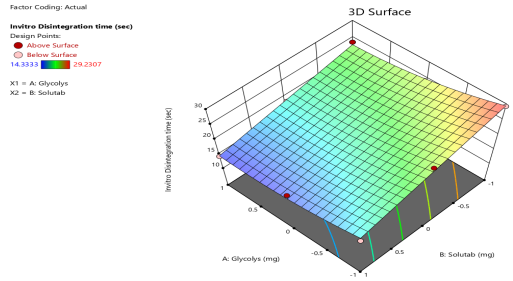

Fig. 5: 3D surface plot showing the effect of Glycolys (X_1) and Solutab (X_2) on *In-vitro* Disintegration time

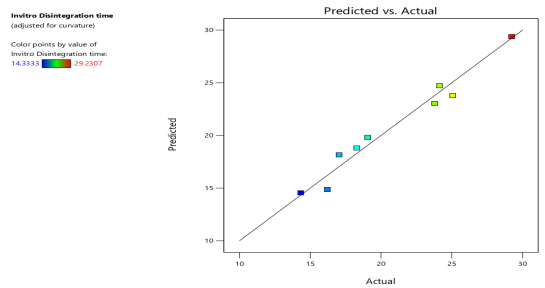

Fig. 6: Graph of Actual value vs Predicted value of *In-vitro* Disintegration Time

The 2D contour plot illustrates the combined influence of Glycolys (B_1) and Solutab (B_2) on *In-vitro* disintegration time. A clear gradient from higher to lower disintegration time is observed as the concentration of both superdisintegrants increases. The closely spaced contour lines indicate a strong effect of formulation variables, while the elliptical nature of the contours confirms interaction between B_1 and B_2. The lowest disintegration time is achieved at higher levels of both factors, validating their synergistic role.

The 3D response surface plot further demonstrates the simultaneous effect of Glycolys and Solutab. The downward sloping surface signifies a progressive reduction in disintegration time with increasing concentrations of both superdisintegrants. The smooth curvature of the surface supports the presence of quadratic behavior and confirms the suitability of the applied quadratic model for optimization.

The predicted versus actual plot shows experimental values closely aligned along the diagonal line, indicating minimal deviation between predicted and observed responses. This confirms the reliability of the developed model and its adequacy in predicting disintegration behavior within the studied design space. Collectively, the graphical analysis substantiates the statistical findings and confirms the effectiveness of Glycolys and Solutab in achieving rapid tablet disintegration.

Statistical Analysis for % CDR at 12 mins

The quadratic model established for percentage cumulative drug release at 12 minutes was statistically significant, as confirmed by the high model F-value and a p-value below 0.05. Both independent variables, **Glycolys (B_1)** and **Solutab (B_2),** exhibited a significant and measurable impact on the drug release behavior

$$Y_2 = 89.50 + 4.34B_1 + 5.95B_2 - 0.7425B_1B_2 + 0.0733B_1^2 + 1.38B_2^2$$

The quadratic polynomial equation explains the influence of **Glycolys (B_1)** and **Solutab (B_2)** on cumulative drug release (% CDR).

The positive coefficients of B_1 and B_2 indicate that increasing the concentration of both superdisintegrants enhances drug release, with Solutab showing a more pronounced effect. The negative interaction term (B_1B_2) suggests a slight antagonistic effect at higher combined levels, while the quadratic terms confirm curvature in the response, justifying the use of a quadratic model.

ANOVA results demonstrate that the model is statistically significant ($p < 0.05$). Both main factors significantly affect % CDR, whereas interaction and quadratic terms are comparatively less influential. The high R^2 value (>0.94) and acceptable adjusted R^2 indicate good model fitness and reliability for prediction. (Fig. 7,8 and 9)

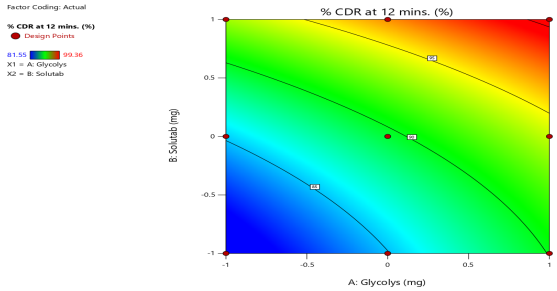

Fig. 7: Contour plot showing the effect of Glycolys (X_1) and Solutab (X_2) on % CDR at 12 mins

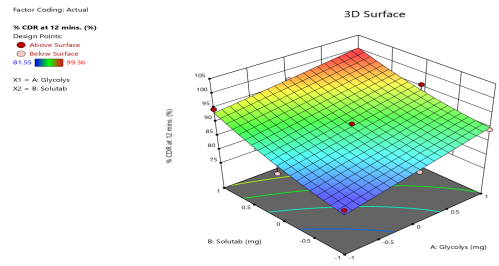

Fig. 8: 3D surface plot showing the effect of Glycolys (X_1) and Solutab (X_2) on % CDR at 12 mins

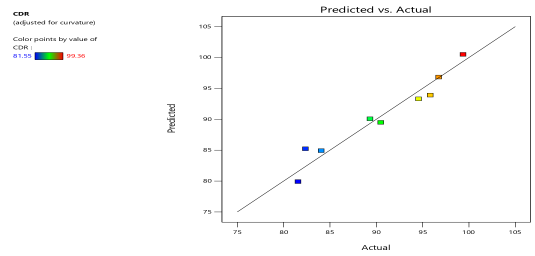

Fig. 9: graph of Actual value vs Predicted value of % CDR at 12 min

The 2D contour plot demonstrates the combined effect of **Glycolys** and **Solutab** on % cumulative drug release. An increase in % CDR is observed with increasing concentrations of both variables. The curved contour lines indicate a nonlinear relationship, confirming the suitability of a quadratic model. Higher Solutab levels show a stronger influence on drug release, while an optimum region is identified where balanced concentrations of both excipients yield maximum % CDR.

The 3D surface plot visually confirms the positive effect of Glycolys and Solutab on % drug release. A smooth ascending surface indicates a good model fit and minimal experimental error. The steeper slope along the Solutab axis highlights its dominant role in enhancing drug release, while the surface curvature supports the presence of interaction and quadratic effects.

The Actual vs. Predicted plot shows close alignment of experimental values with predicted values along the diagonal line. This indicates strong agreement between observed and model-predicted % CDR, confirming the accuracy, reliability, and predictive capability of the developed quadratic model.

Stability study

The stability study of the optimized batch BS9 was conducted under accelerated conditions (40 ± 2 °C and 75 ± 5 % RH) for one month to evaluate the effect of storage on its quality attributes. The results showed negligible changes in physical parameters such as hardness, wetting time, and in-vitro disintegration time compared to the initial values, indicating that tablet integrity and rapid disintegration properties were maintained. In-vitro drug release profile after one month was almost identical to the initial profile, with only a slight variation observed, demonstrating that storage conditions did not significantly affect dissolution behaviour. Overall, the findings confirm that batch BS9 remains stable under accelerated conditions, maintaining its physical properties, drug content, and dissolution performance, thus supporting its suitability for further development and commercialization. (Table 11 and 12, Fig 10)

Table 11: Result of the Stability study

Sr.	Evaluation parameter	Results of optimized batch BS9	Result after 1 month at 40° ± 2 °C and 75 ± 5 % RH
1	**Hardness (kg/cm^2)**	2.17 ± 0.29	2.43 ± 0.06
2	**Wetting Time (sec.)**	12.19 ± 0.12	12.05 ± 0.07
3	***In-vitro* Disintegration Time (sec.)**	14.33 ± 0.58	13.99 ± 0.13
4	**Drug Content (%)**	98.59 ± 0.57	98.33 ± 0.14

Table 12: *In Vitro* Drug Release Study of Stability Batch

Time (Min.)	% CDR of Optimized Batch BS9 Initially (%)	% CDR of batch BS9 After Time Period of 1 Month (%)
0	0	0
2	58.26	57.85
4	69.93	68.15
6	81.17	80.26
8	92.56	90.48
10	97.26	95.76
12	99.36	98.92

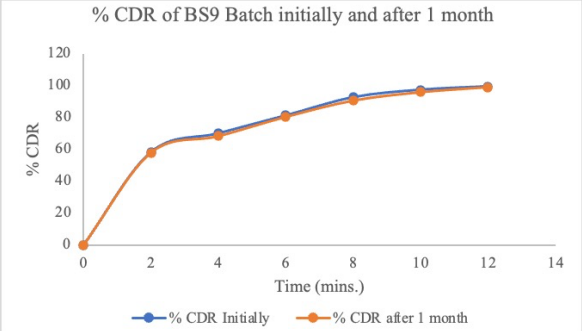

Fig. 10: Comparison of *In Vitro* Drug Release study of Optimized batch and Stability batch

CONCLUSION

The present study focused on the formulation and optimization of sublingual tablets of Buspirone HCl to achieve rapid disintegration and enhanced drug release. Preformulation studies confirmed the identity, purity, and compatibility of the drug with selected excipients through melting point determination, UV spectrophotometry. Formulations (BS1–BS9) prepared with superdisintegrants showed acceptable pre- and post-compression parameters, with tablets exhibiting suitable hardness, low friability, and uniform drug content. Formulations containing Solutab demonstrated faster wetting and disintegration compared to other superdisintegrants. A 3^2 factorial design using Glycolys (X_1) and Solutab (X_2) was applied to optimize the formulation, producing factorial batches (BS1–BS9) with satisfactory characteristics. Among them, batch BS9 showed the best performance with rapid disintegration and 99.36% drug release within 12 minutes. Statistical analysis (ANOVA) confirmed significant models with high R^2 values, indicating reliable optimization. Stability studies of the optimized batch under accelerated conditions showed negligible changes in physical parameters, drug content, and dissolution profile, confirming formulation stability. Overall, the study demonstrated that the combination of Glycolys and Solutab effectively produces rapidly disintegrating sublingual tablets of Buspirone HCl with potential for improved therapeutic efficacy and future commercial development.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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