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A STATISTICAL APPROACH TO THE DEVELOPMENT OF FAST DISINTEGRATING TABLETS OF TELMISARTAN USING CO-PROCESSED SUPERDISINTEGRANT

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Keywords:

Box Behnken design, Factorial design, Fast disintegrating tablets, Telmisartan

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ABSTRACT: The present investigation deals with fast disintegrating tablets of the model drug (Telmisartan) and to determine the influence of the excipients on physical properties of tablets. Employing a Box Behnken design, concentration of co-processed superdisintegrants (Crosspovidone: sodium starch glycolate) (X_1), the concentration of meglumine (X_2) and concentration of sodium lauryl sulfate (X_3), selected as independent variables whereas disintegration time (Y_1) selected as the dependent variable. All formulations were evaluated for pre-compression and post-compression parameters. Mathematical equations and response surface plots were used to relate the dependent and independent variables. The regression equation generated for disintegration time (DT) of Telmisartan tablets was Y_1=30.25-1.6887A-1.2175B +2.7437C +0.1675AB +2.02AC+3.007BC-2.6752A^2-3.62B^2+ 0.0425C^2. The statistical validity of the polynomial was established, and optimized formulation factors were selected by feasibility and grid search. Validation of the optimization study with 13 confirmatory runs indicated a high degree of prognostic ability of response surface methodology.

INTRODUCTION: Oral drug delivery remains the most preferred route for administration of various therapeutic agents. Recent advances in technology prompted researchers and scientists to develop oral disintegrating tablets (ODT) with improved patient convenience and compliance. ODTs are solid unit dosage form which dissolves or disintegrate rapidly in the mouth without water or chewing [1]. Novel ODT technologies address many patient and pharmaceutical needs such as enhanced life cycle management to convenient dosing, particularly for pediatric, geriatric, and psychiatric patients who have difficulty in swallowing (Dysphagia) conventional tablet and capsules.

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Technologies used for manufacturing of ODTs are either conventional technologies or patented technologies [2]. Telmisartan is a potent, long-lasting, nonpeptide antagonist of angiotensin II (AT1) receptor blocker (ARB), which is indicated for the treatment of hypertension. It blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II [3, 4]. It is practically insoluble in water and soluble in strong base. It has the longest half-life of any ARB (24 h). It is also used to treat congestive heart failure and prevent strokes, heart attacks, and kidney damage due to diabetes.

Telmisartan is a nonpeptide angiotensin receptor (Type- AT) antagonist, that cause inhibition of the action of angiotensin II onthe vascular smooth muscle in the symptomatic treatment of hypertension. The bioavailability of Telmisartan is poor about 45%, which due to extensive first-pass hepatic metabolism [5]. The bioavailability can be increase by fast dissolving formulation. Conventional Telmisartan tablets available in the market are not suitable where the quick onset of

action is required [6]. Traditional experiment requires more effort, time, and materials when a complex designs are useful in optimizing formulations, requiring less experimentation and providing estimates of the relative significance of different variables.

Response surface methodology (RSM) is a widely practiced approach in the development and optimization of drug delivery devices [7]. In this investigation, we explored the utility of RSM for the optimization of tablets. Based on the principle of design of experiments, the methodology encompasses the use of various types of experimental designs, generation of polynomial equations, and mapping of the response over the experimental domain to optimize the tablets. The technique requires minimum experimentation and time, thus providing to be far more effective and cost-effective than the conventional methods of formulating dosage forms [8, 9].

The work reported in this paper; a Box Behnken design was used to optimize tablets containing Telmisartan drug. Independent variables selected were co-processed superdisintegrant (X_1), meglumine (X_2) and sodium lauryl sulfate (SLS) (X_3) to evaluate their separate and combined effects on disintegration time as the dependent variable.

MATERIALS AND METHODS:

Materials: Telmisartan was procured from Yarrow Chemicals, Mumbai, India. All other chemicals were of analytical grades.

Methods:

Preparation of Co-processed Super-disintegrants: [10-13] The co-processed super-disintegrants were prepared by solvent evaporation methods. A blend of crospovidone: sodium starch glycolate (in the ratio of 1:1, 1:2, 1:3) was added to 10 ml of ethanol. The contents were mixed thoroughly and stirred continuously until most of the ethanol evaporated. The wet coherent mass granulated through #40 mesh sieve. The wet granules were dried in a hot air oven at 60 ºC for 20 min. The dried granules were sifted through #44 mesh sieve and stored in an airtight container until further use.

Preparation of Tablets Using Factorial Designs: [9, 14, 15] To the weighed quantity of water dissolve dispensed quantity of sodium hydroxide pellets followed by Telmisartan and meglumine. Stir the resultant solution until yellowish solution is obtained. Granulate the sifted quantity of microcrystalline in RMG using a yellowish solution of drug with other excipients. Dry these granules at 60 ± 10 ºC. Pass the dried granules through #20 sieve. Finally, co-processed super disintegrant, crospovidone XL and magnesium stearate were added and mixed well for 5 min in a blender and collected for compression.

A Box Behnken design was employed to study the effect of independent variables on dependent variables, as shown in **Table 1**. The prepared granules were evaluated for pre-compression parameters, and the prepared tablets were evaluated for post-compression parameters.

Experimental Design: [3, 8, 9, 14, 15] Box Behnken statistical screening was used to statistically optimize the formulation factors and evaluate main effects, interaction effects, and quadratic effects on the disintegration time. RSM such as Box Behnken model possible curvature in the response function. A three-factor, three-level Box Behnken design was used to explore quadratic response surface and to construct second order polynomial models with Design Expert (Version 11.1.2.0, Stat-Ease Inc. Minneapolis, MN, USA). The Box Behnken cubic design is characterized by a set of points lying at the midpoint of each edge of a multidimensional cube and center point replicates (n=3), whereas the "missing corners" help the experimenter to avoid the combined factor extreme. A design matrix comprising of 13 experimental runs was constructed.

The non-linear computer generated quadratic model is given as $Y=b_0+b_1X_1+b_2X_2+b_3X_3+b_{12}X_1X_2+b_{13}X_1X_3+b_{23}X_2X_3+b_{11}X_1^2+b_{22}X_2^2+b_{33}X_3^2$ where Y is the measured response associated with each factor level combination: b_0 is constant; b_1, b_2, b_3 are linear coefficients, b_{11}, b_{22}, b_{33} are quadratic coefficients computed from experimental runs; and X_1, X_2, and X_3 are coded levels of independent variables. The term X_1X_2 and X_i^2 (i = 1, 2 or 3) represent the interaction and quadratic terms, respectively. The independent variables selected were the amount of Co-processed superdisintegrant (X_1), meglumine (X_2), SLS (X_3).

The dependent variable was disintegration time (Y_1) with constraints applied to the formulation of tablets. The concentration range of independent variables was selected based on the following observations from preliminary experimentation. The selected concentration range of independent variables under study with their low, medium, and high levels are shown in **Table 1**.

TABLE 1: VARIABLES AND OBSERVED RESPONSES IN BOX-BEHNKEN DESIGN FOR TABLET

Batch	Independent variables			Dependent variable	The level used, Actual (Coded)		
	X_1	X_2	X_3	Y_1 (Sec)	Low (-1)	Medium (0)	High (+1)
1	-1	-1	0	26.44			
2	1	-1	0	24.35			
3	-1	1	0	23.23			
4	1	1	0	21.81			
5	-1	0	-1	29.12			
6	1	0	-1	20.08			
7	-1	0	1	31.12			
8	1	0	1	30.16			
9	0	-1	-1	28.21			
10	0	1	-1	20.20			
11	0	-1	1	27.13			
12	0	1	1	31.15			
13	0	0	0	30.25			
Independent variables							
X_1 = Co-Processed Superdisintegrant					1:1	1:2	1:3
X_2 = Meglumine (%)					0	2.5	5
X_3 = SLS (%)					0	2.5	5

Evaluation of Pre-compression Parameters: [16, 17]
The prepared granules were evaluated for parameters like bulk density, tap density, carr index, angle of repose, and Hausner's ratio. The observation recorded in **Table 2**.

Bulk and Tapped Density: Both bulk and tapped densities were determined and expressed in gm/cm^3. The bulk density and tapped density were calculated using the following equations

$$\text{Bulk density (Bd)} = M/Vo$$

Where, M= mass of powder taken, Vo = apparent unstirred volume.

$$\text{Tapped density (Td)} = M/Vf$$

Where, M= weight of sample powder taken, Vf = tapped volume.

Compressibility Index: The Compressibility index of the powder blend was determined by Carr's Compressibility index. The formula for Carr's index is as below.

$$\text{Carr's Index} = \{Td\text{-}Bd) / Td\} \times 100$$

Where, Td = tapped density, Bd = bulk density.

Hausner Ratio: The Hausner ratio is an index of ease of powder flow. It is calculated by the following equation.

$$\text{Hausner ratio} = Td / Bd$$

Where, Td = tapped density, Bd = bulk density.

Angle of Repose: The angle of repose of powder blend was determined according to fixed funnel and free-standing cone method. The angle of repose (θ) was calculated using the following equation.

$$\tan \theta = H/R$$

Therefore, Angle of repose = $\tan \theta^{-1}$ (H /R). Where, H = height of the powder cone, R = radius of the powder cone.

Evaluation of Post-compression Parameters:[16-18]
Weight Variation Test: To find out weight variation, 20 tablets of each type of formulations were weighed individually using an electronic balance, the average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

Thickness: The thickness of the tablets was determined using a Micrometer screw gauge. Five tablets from each type of formulations were used, and average values were calculated. It is expressed in mm.

Hardness: The resistance of tablets to shipping, breakage, under conditions of storage,

transportation, and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured.

Friability: Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. A sample of pre-weighed 10tablets was placed in Roche friabilator which was then operated for 100 revolutions, *i.e.* 4 min. The tablets were then dusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable. Percent friability (% F) was calculated as follows:

% Friability = Weight before friabilation - Weight after friabilation / Weight before friabilation × 100

Uniformity of Drug Content: Five tablets of each type of formulation were weighed and crushed in mortar and powder equivalent to 40mg of Telmisartan was weighed and dissolved in 100ml of 0.1N HCl (pH 1.2) This was the stock solution from which the 1ml sample was withdrawn and diluted to 10 ml with 0.1N HCl (pH 1.2). The absorbance was measured at wavelength 291 nm using UV-Visible spectrophotometer (Shimadzu, 1700, Japan). Content uniformity was calculated using the formula:

$$\% \text{ Purity} = 10 \times C \times (Au/As)$$

Where, C=Concentration, Au, and As=Absorbance of unknown and standard respectively.

Wetting Time: A piece of tissue paper folded twice containing amaranth powder on the upper surface was placed in a small Petri dish containing 6ml of 0.1N HCl, a tablet was put on the paper and the time required for the formation of pink color was measured as wetting time. The study was performed in triplicate.

Water Absorption Ratio: A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then weighed. Water absorption ratio (R) was determined using the following equation:

$$R = (Wb-Wa)/ Wa \times 100$$

Where, Wa = Weight of the tablet after wetting, Wb = Weight of the tablet before wetting.

Disintegration Time: Initially, the disintegration time for tablets was measured using the conventional test for tablets as described in the pharmacopeia. Tablets were placed in disintegration tube and time required for complete disintegration *i.e.* without leaving any residues on the screen was recorded as disintegration time. A modified method was used to check the disintegration time. In about 6-8 ml of 0.1N HCl (pH 1.2) was taken in measuring cylinder. Tablet was placed in the cylinder, and complete dispersion of tablet in the cylinder was recorded as the disintegration time.

***In-vitro* Dissolution Study:** The release rate of Telmisartan from fast disintegrating tablets was determined using the United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl dissolution medium, at 37 ± 0.5 °C and 75 rpm. 10 ml samples were withdrawn at predetermined time intervals and replaced with same dissolution media. The samples were withdrawn and analyzed by using UV spectrophotometer at λ_{max} 291 nm.

RESULTS AND DISCUSSION:

Evaluation of Pre-compression Parameters: Fast disintegrating tablets of Telmisartan were prepared using the above co-processed superdisintegrants. Co-processed superdisintegrants were prepared by solvent evaporation using crospovidone and sodium starch glycolate in different ratios (1:1, 1:2 & 1:3). A total of thirteen formulations were designed and evaluated for pre-compression parameters. As the blends were free-flowing (angle of repose <25º, Hausner ratio 1.10-1.14, and Carr's index 10-15% **Table 2**).

Evaluation of Post-compression Parameters: All the post-compression parameters are evaluated were in prescribed limits, and results were within IP acceptable limits. Results of post-compression parameters were shown in **Table 4**. The weight variation was found in all designed formulations in the range 198 to 200 mg. All the tablets passed weight variation test as the average percentage

weight variation was within 7.5%, *i.e.* in the pharmacopeia limits. The standard deviation values indicated that all the formulations were within the range. The thickness of tablets was found to be in the range of 3.06 to 3.17 mm. In all the formulations, the hardness test indicated good mechanical strength ranges from 3.8 to 4.5 kg/cm^2. The friability range is 0.68 to 0.89% to be well within the approved range (<1%) indicated that the tablet had good mechanical resistance. The drug content uniformity was in between 97.46 to 101.1%, water absorption ratio was found between 45 to 75 and wetting time between 69 to 111sec. Rapid disintegration within several mins was observed in all the formulations.

TABLE 2: MICROMETRIC PROPERTIES FOR FORMULATION BLENDS

Parameters	Bulk Density (g/cm3)	Tapped Density (g/cm^3)	Carr's Index (%)	Angle of Repose (º)	Hausner Ratio
1	0.531	0.608	12.66	25.02	1.1450
2	0.521	0.616	15.42	26.18	1.1823
3	0.512	0.609	15.92	25.12	1.1894
4	0.523	0.611	14.40	28.63	1.1682
5	0.527	0.614	14.82	24.44	1.1650
6	0.524	0.618	15.21	26.04	1.1793
7	0.519	0.612	15.19	26.18	1.1791
8	0.521	0.613	15.00	25.91	1.1765
9	0.523	0.608	13.98	27.11	1.1625
10	0.527	0.613	14.02	25.02	1.1631
11	0.521	0.607	14.16	26.91	1.1650
12	0.531	0.614	13.51	25.44	1.1563
13	0.521	0.613	15.00	25.91	1.1765

TABLE 3: POST COMPRESSION PARAMETERS OF TELMISARTAN TABLET FORMULATION

Parameters	Weight variation (mg ± SD)	Thickness (mm ± SD)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
1	200±0.2	3.12±0.20	3.9±0.45	0.68±0.12	98.29±0.31
2	198±0.2	3.10±0.10	4.2±0.22	0.89±0.11	99.43±0.13
3	199±0.1	3.06±0.20	3.8±0.34	0.72±0.12	100.3±0.21
4	198±0.1	3.14±0.14	3.8±0.45	0.74±0.15	101.1±0.25
5	198±0.2	3.12±0.11	4.1±0.44	0.83±0.17	97.46±0.27
6	200±0.1	3.08±0.13	4.2±0.38	0.79±0.20	98.76±0.34
7	200±0.2	3.12±0.18	4.5±0.31	0.70±0.21	97.92±0.21
8	198±0.3	3.11±0.07	3.9±0.35	0.82±0.20	99.39±0.15
9	199±0.2	3.17±0.07	4.0±0.38	0.75±0.19	98.91±0.35
10	198±0.2	3.11±0.11	3.8±0.28	0.85±0.17	98.32±0.21
11	200±0.1	3.12±0.13	3.9±0.41	0.69±0.15	97.92±0.27
12	200±0.1	3.07±0.15	4.5±0.41	0.73±0.11	98.43±0.11
13	200±0.1	3.11±0.11	4.3±0.37	0.81±0.15	99.28±0.35

TABLE 4: POST COMPRESSION PARAMETERS OF TELMISARTAN TABLET FORMULATION

Parameters	Wetting Time (Sec)	Water Absorption Ratio	Disintegration Time (Sec)	Drug Release (%)
1	69±1.37	52±0.32	16.44±2.36	82.54±0.31
2	83±1.13	60±0.15	24.35±1.36	76.39±0.46
3	76±1.54	62±0.22	13.23±1.59	67.59±0.12
4	81±1.23	54±0.13	21.81±1.28	92.55±0.38
5	62±2.09	45±0.43	29.12±1.53	85.01±0.18
6	81±1.37	59±0.21	18.08±1.39	74.45±0.57
7	98±1.54	61±0.29	31.12±2.09	65.87±0.33
8	111±1.53	67±0.12	30.16±1.43	84.76±0.22
9	95±1.23	75±0.11	28.21±1.23	93.65±0.38
10	76±1.28	87±0.13	20.20±1.54	72.51±0.30
11	88±1.12	54±0.23	27.13±1.53	68.62±0.22
12	95±1.38	48±0.35	31.15±1.37	87.73±0.29
13	87±1.45	55±0.43	30.25±1.52	96.84±0.32

The *in-vitro* disintegration time of fast disintegrating tablets was found to be 13.23 to 31.15 sec, which is in the range of fulfilling the official requirements. By the addition of superdisintegrants the disintegration time increased significantly (P<0.05) tablets prepared. All the results were given in **Table 3**, **4**.

Experimental Design: The independent variables and the responses for all 13 experimental runs are given in Table1. The 13 experimental formulations of tablets were prepared using co-processed superdisintegrant. The responses, disintegration time (Y_1) was found to be significantly higher 31.15sec only when co-processed superdisintegrant was used at medium and meglumine, sls were used at high concentration level, respectively. The response, Y_1 varies from 20.08 to 31.15 sec. For estimation of the quantitative response of these model, formulations ranged from a less disintegration time to high disintegration time. For estimation of quantitative effects of the different combination of factors and the factor levels on the disintegration time, the response models were calculated with Design Expert software by applying coded values of factor levels. The model described could be represented as:

Coded level: Disintegration time (Y_1) = 30.25 - 1.6887A -1.1275B +2.7437C +0.1675AB +2.02AC +3.007BC -2.6752A^2 -3.62B^2 +0.0425C^2..... 1

Fitting of Data to the Model: A three-factor, three-level Box-Behnken statistical experimental design as the RSM requires 13 experiments. Formulation 13 showed a significantly better disintegration time among the experimental runs. All the responses observed for 13 formulations prepared were simultaneously fit first order, second order, and quadratic models using Design Expert 11.1.2.0. It was observed that the best fit model was the quadratic model, and Sum of squares is Type III -partial. A positive value represents an effect that favors the optimization, while a negative value indicates an inverse relationship between the factor and response. It is evident that all the three independent variables, *viz.* the Co-processed superdisintegrant (X_1), meglumine (X_2) and SLS (X_3) have positive effects on the response, *viz.* disintegration time. The quantitative effects of the different combination of factors and factor levels on the disintegration time were calculated using response surface models. The significant p-value ($p<0.05$), R^2, adjusted R^2, and coefficient of variation values of this model indicated that the assumed regression model was significant and valid for each considered response. The values of the coefficients in the model are related to the effect of these variables on the response. Form this model quadratic was best, indicating that the combination of the above system had the greatest potential influence on the Telmisartan fast disintegrating tablet. The 3-D response surface **Fig. 1** was drawn to estimate the effects of the independent variables on response and to select the optimal formulation.

Data Analysis: The disintegration time (dependent variable) obtained at various levels of the three independent variables (X_1, X_2, and X_3) was subjected to multiple regression to yield a polynomial equation. The value of the correlation coefficient (r^2) of the equation was found to be 0.9684, indicating a good fit. VIF value found to be 1, indicating the model is significant.

According to **Table 5**, the result calculated using equation 1 was statistically significant with $p<0.005$, indicating that the developed model exhibited good agreement between the response Y_1 and the significant variables. The value of lack of fir for the equation more than 0.05 indicating that the proposed statistical model fit well. The ANOVA result for Y_1 provides F value 10.24 as compared to the critical values from the cut-off point for F distribution (=0.05) **Table 5**. These F value suggested that the derived quadratic models have a significant influence on the response R^2 and adjusted R^2 value for Y1 were 0.9684, 0.8739, respectively demonstrate the accuracy of the test and the fitness of the results with the prepared model.

The disintegration time measured for the different formulations showed wide variation (*i.e.*, values ranged from 20.08 to 31.15 sec). The results indicate that the disintegration time is strongly affected by the variables selected for the study. The main effects of X_1, X_2, and X_3 represent the average result of changing one variable at a time from its low level to its high level. The interaction terms (X_1X_2, X_1X_3, X_2X_3, X_1^2, X_2^2, X_3^2) shows how the disintegration time changes when two variables

are simultaneously changed. The negative coefficient for all three independent variables an unfavorable effect on the disintegration time, while positive coefficients for the interactions between two variables indicate a favorable effect on disintegration time.

TABLE 5: SUMMARY OF ANOVA FOR RESPONSE Y_1 FOR FITTING TO QUADRATIC MODEL

Source	Model	A	B	C	AB	AC	BC	A^2	B^2	C^2	Residual	Core Total
Sum of Squares	192.45	22.82	11.86	60.23	0.1122	16.32	36.18	16.33	29.95	0.0041	6.26	198.71
Degree of Freedom	9	1	1	1	1	1	1	1	1	1	3	12
Mean Square	21.38	22.82	11.86	60.23	0.1122	16.32	36.18	16.33	29.95	0.0041	2.09	-
f-value	10.24	10.93	5.68	28.85	0.0538	7.82	17.33	7.82	14.35	0.0020	-	-
p-value	0.0406	0.455	0.0973	0.0216	0.8316	0.0681	0.0252	0.0681	0.0323	0.9673	-	-
Coefficient estimates	30.25	-1.69	-1.22	2.74	0.1675	2.02	3.01	-2.67	-3.62	0.0425	-	-
Standard Error	1.44	0.5108	0.5108	0.5108	0.7224	0.7224	0.7224	0.9557	0.9557	0.957	-	-
95% CL Low	25.65	-3.31	-2.84	1.12	-2.13	-0.2791	0.7084	-5.71	-6.66	-3.00	-	-
95% CL High	34.85	-0.0631	0.4082	4.37	2.47	4.32	5.31	0.3689	-0.5786	3.08	-	-
Std. Deviation		1.4448			CV%		5.4720		R^2		0.9684	
Pred. R^2		0.6638			Adjusted R^2		0.8739		Mean		26.40	

Counterplots and Response Surface Analysis: Two-dimensional counterplots and 3-D response plots are shown in **Fig 1A**, **1B**, **1C,** and **Fig. 2A**, **2B**, **2C**, which are very useful to study the interaction effects of the factors on the responses. These types of plots are useful in the study of the effects of two factors on the response at one time.

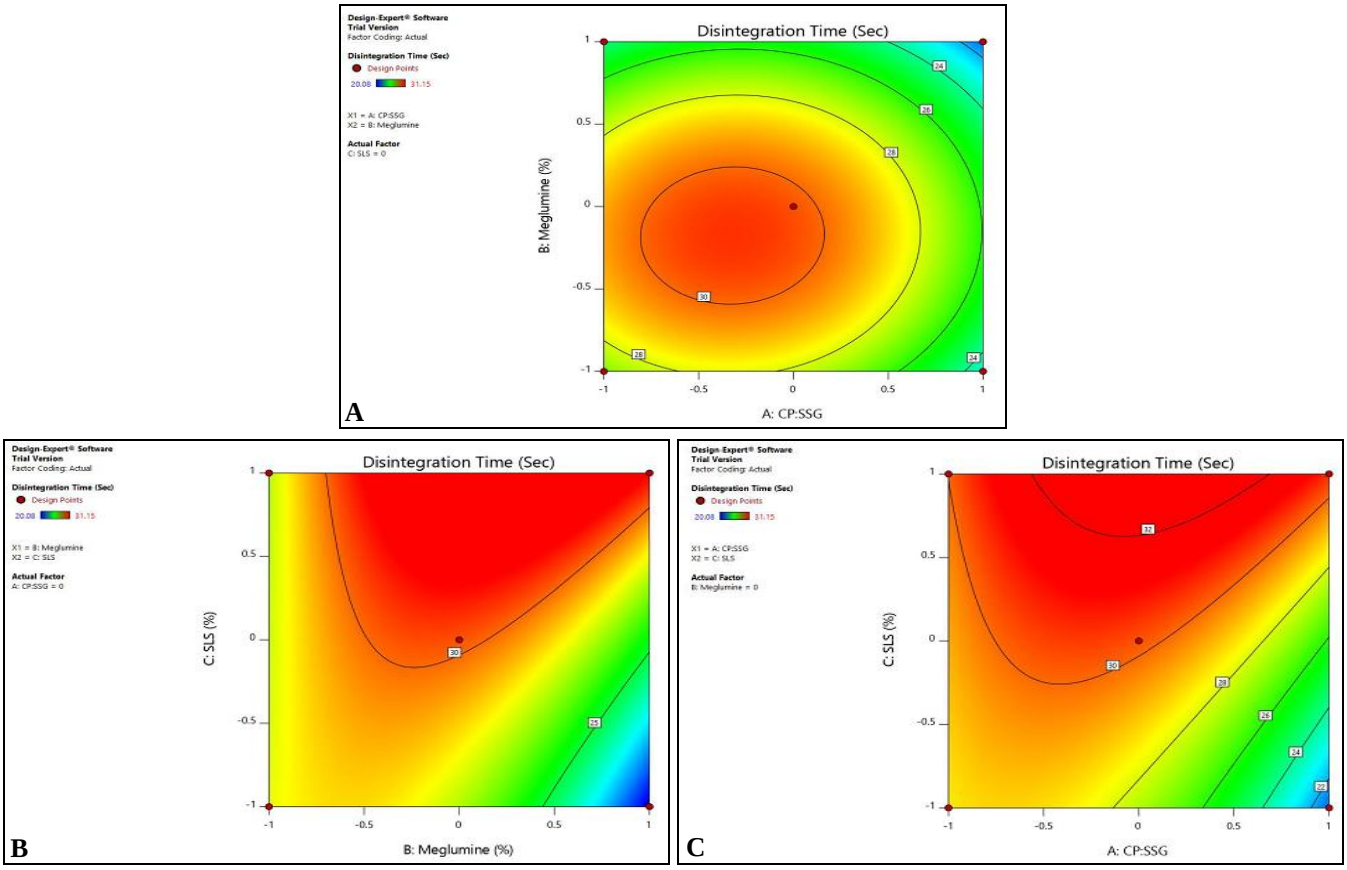

FIG. 1: (A) COUNTERPLOT SHOWING EFFECT MEGLUMINE AND CO-PROCESSED SUPERDISINTEGRANT ON RESPONSE Y_1 (B) COUNTERPLOT SHOWING EFFECT SLS AND MEGLUMINE ON RESPONSE Y_1 (C) COUNTERPLOT SHOWING EFFECT SLS AND CO-PROCESSED SUPERDISINTEGRANT ON RESPONSE Y_1

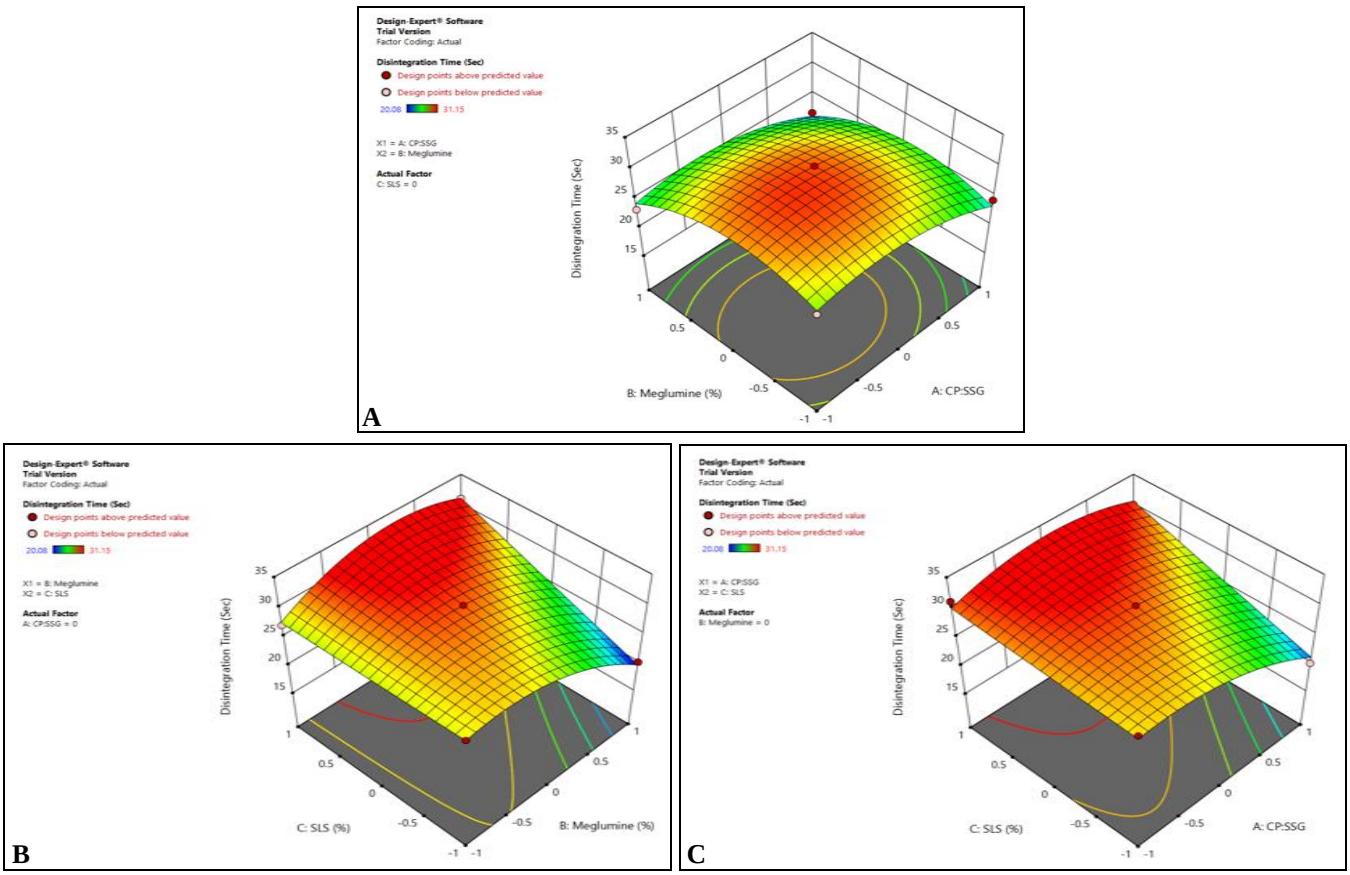

FIG. 2: (A) RESPONSE SURFACE PLOT SHOWING EFFECT MEGLUMINE AND CO-PROCESSED SUPERDISINTEGRANT ON RESPONSE Y_1 (B) RESPONSE SURFACE PLOT SHOWING EFFECT SLS AND MEGLUMINE ON RESPONSE Y_1 (C) RESPONSE SURFACE PLOT SHOWING EFFECT SLS AND CO-PROCESSED SUPERDISINTEGRANT ON RESPONSE Y_1

In all the presented figures, the third factor was kept at a constant level. All the relationships among the three variables are non-linear, although they exhibit a nearly linear relationship of factors.

Optimization: The optimum formulation was selected based on criteria of attaining a maximum value of disintegration time by applying constraints on Y_1.

Upon trading of various response variables and comprehensive evaluation of feasibility search and exhaustive grid search, the formulation 13 was found to fulfill the maximum requisite of an optimum formulation because of maximum disintegration time values **Table 6**.

Validation of Response Surface Methodology: 13 formulations were obtained from RSM, the composition and predicted the response of which are listed in **Table 5**. To confirm the validity of the optimal calculated parameters and predicted responses, the optimum formulations were prepared according to the above value of the factors. From the results presented in **Table 5**, the predicted error is below 15%, indicating that the observed responses were very close to the predicted values, shown in **Table 6**. The linear correlation plots were drawn between the predicted and experimental values. Thus, the low magnitudes of error, as well as the R2 values in the present investigation, prove the high prognostic ability of the RSM.

TABLE 6: SIMULTANEOUS OPTIMAL SOLUTION BY RSM

Response	Pred. Mean	Pred. Median	Observed	Std. Deviation	SE Mean	95% CL Low	95% CL High	95%TL Low	95% High
DT	30.25	30.25	31.26	1.4484	1.4484	25.6579	34.8481	15.9824	44.5176

CONCLUSION: The data obtained from the study of "A statistical approach to the development of fast disintegrating tablets of Telmisartan using co-processed superdisintegrant" reveals conclusion

that use of co-processing of superdisintegrants significantly enhances the disintegration time of Telmisartan tablets. After the determination of significant parameters by using Box Behnken design methodology was applied.

Analytical parameters investigated in this study were: concentration of superdisintegrants (X_1), meglumine (X_2) and SLS (X_3). The chosen response was disintegration time. The levels of these factors were predicted to obtain an optimal response concerning set constraints. It is essential that experimental design methodology is a very economical way for extracting the maximum complex information, a significant experimental time-saving factor, and it saves the material used for analyses and personal cost as well. It is concluded that by adopting a systematic formulation approach, an optimum can be reached in the shortest time with minimum efforts.

Future Prospective: Co-processing of super-disintegrants proven an ideal way for the formulation of the fast disintegrating tablet of Telmisartan. As co-processing of excipients shows better dissolution than that of alone superdisintegrants used in formulation.

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CONFLICT OF INTEREST: Nil

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