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# Formulation and evaluation of orally disintegrating tablet of Rizatriptan using natural superdisintegrant

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**ABSTRACT**

**Introduction:** Rizatriptan benzoate is a potent and selective 5-$HT_{1B/1D}$ receptor agonist and is effective for the treatment of acute migraine. Difficulty in swallowing is common among all age groups, especially elderly and pediatrics. Orally disintegrating tablets may constitute an innovative dosage form that overcome the problem of swallowing and provides a quick onset of action. This study was aimed to formulate and evaluate an Orally Disintegrating Tablet (ODT) containing Rizatriptan while using semi-synthetic and natural superdisintegrants.

**Methods:** Orodispersible tablets were prepared by direct compression using natural superdisntegrant (Plantago ovata mucilage) and semi-synthetic superdisntegrant (crospovidone). The prepared tablets were evaluated for hardness, friability, thickness, drug content uniformity, water absorption and wetting time. A $3^2$ factorial design was used to investigate the effect of independent variables (amount of crospovidone and Plantago ovata mucilage) on dependent variables [disintegration time, wetting time and $Q_5$ (cumulative amount of drug release after 5 minutes)]. A counter plot was also presented to graphically represent the effect of independent variable on the disintegration time, wetting time and $Q_5$. The check point batch was also prepared to prove the validity of the evolved mathematical model. The systematic formulation approach helped in understanding the effect of formulation processing variable.

**Results:** According to the results of optimized batches, the best concentration of superdisintegrant were as follows: 9.4 mg Psyllium mucilage and 8.32 mg crospovidone gave rapid disintegration in 35sec and showed 99% drug release within 5 minutes.

**Conclusion:** Plantago ovata mucilage, a natural superdisintegrant, gives a rapid disintegration and high release when used with synthetic superdisntegrant in formulation of orally disintegrating tablet of Rizatriptan.

*Implication for health policy/practice/research/medical education:*
Plantago ovata mucilage is a natural superdisntegrant that has shown a good disintegration time and wetting effect when used with synthetic superdisntegrant in formulation of orally disintegrating tablet of Rizatriptan.
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## Introduction

Drug delivery through oral route is the most common and preferred route of drug administration both for solid and liquid dosage forms. However, solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance, and most importantly the patient compliance (1). Tablets and capsules are the most popular solid dosage forms. However, many people face difficulty in swallowing tablets and hard gelatin capsules (2). It has been found that this problem has been encountered in all groups of patient, but especially with pediatric and geriatric populations. Thus, these conventional dosage forms result in high incidence of noncompliance and ineffective therapy with respect to swallowing specially in the case of pediatric, geriatric, or any mentally retarded persons (3).

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It offers several advantages with respect to its stability, administration without water, accurate dosing, easy manufacturing, small packaging size, and handling (4). Its ease of administration in the population especially for pediatric, geriatric, or any mentally retarded persons makes it a very popular dosage form. Due to the presence of superdisintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which in turn provides rapid onset of action (5).

Rizatriptan has a high oral bioavailability of 45%. The half-life is 2 to 3 hours and the $T_{max}$ is 1.5 hours for the conventional tablet and slightly longer for the ODT. 10 mg dose of Rizatriptan benzoate is equipotent to a 100 mg of Sumatriptan, the traditional anti migraine drug. The bioavailability of Rizatriptan benzoate is about 45% which is superior to a poor 14-17% of Sumatriptan (6,7).

In market Rizatriptan is available in freeze dried dosage form which gives rapid disintegration. Main disadvantage of this method is very costly method, process is not feasible and product is highly sensitive to moisture. Freeze drying is cumbersome and it yields a fragile and hygroscopic product (8).

In this study natural superdisintegrants were utilized. Natural superdisintegrants are safer, more biodegradable, better compressible, easier to preparation and cheaper and these advantages can boost the production of ODTs (9).

In the present study, the fast disintegrating tablets were prepared by the method of direct compression using various pharmaceutical excipients. The excipients used were avicel pH 102,
crospovidone, Plantago ovata mucilage, mannitol, aspartame, aerosil and magnesium stearate.

## Materials and Methods

Rizatriptan benzoate was bought from Farabi Pharmaceutical Company. Aerosil and aspartame was obtained as gift from Isfahan University of Medical Science Lab and other ingredients were bought from market.

### *Preparation of orally disintegrating tablets*

Orally disintegrating tablet of Rizatriptan was prepared by direct compression method. All the ingredients were passed through 60 mesh sieve separately. The Rizatriptan, crospovidone, Psyllium mucilage, avicel PH 102, mannitol and aspartame were mixed up using a mortar and pestle. The blends were lubricated with 1% magnesium stearate and 1% aerosil. The blends ready for compression were converted into tablets. Tablets were compressed at 3 mm size flat round punch to get tablet machine (ErwekaAR 4100, Germany). The compositions of experimental factorial design were shown in Table 1.

### *Methodology for isolation of Plantago ovata mucilage*

For the isolation of mucilage, seeds of Plantago ovata were used. They were soaked in distilled water for 48 h and then boiled for 1 h for complete release of mucilage into water. The material was filtered by squeezing in a muslin cloth to remove marc. Then equal volume of acetone was added to filtrate to precipitate the mucilage. The mucilage was separated and dried in oven at a temperature less than 60°, powdered (#60 mesh), weighed and stored in desicator until further use (10).

### *$3^2$ full factorial design*

Response surface methodology (RSM) was characteristically employed to relate a response variable to the levels of the input variables and to generate a design matrix to choose the optimal formulations. A statistical model, which consisted of interactive and polynomial terms, was utilized to evaluate the responses (11,12). The responses were analyzed using analysis of variance (ANOVA) and the individual response parameters were evaluated using F test and polynomial equation was generated for each response using multiple linear regression analysis.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2$$

Where, Y is the dependent variable, $b_0$ is the arithmetic mean response of the nine runs and $b_1$ is the estimated coefficient for the factor $X_1$. The main effects ($X_1$ and $X_2$) represent the average result of changing one factor at a time from its low to high value. The interaction terms ($X_1$ $X_2$) show how the response changes when two factors are simultaneously changed. The polynomial terms ($X_1^2$ and $X_2^2$) are included to investigate non-linearity. A $3^2$ full factorial design was employed to study the effect of independent variables, i.e., amount of mucilage ($X_1$) and the amount of crospovidone ($X_2$) on dependent variables wetting time, disintegration time and $Q_5$ (cumulative amount of drug release after 5 minutes).

After application of full factorial design and with the help of produced polynomial terms, amount of two formulation variable was optimized. The optimized amount of the crospovidone and Psyllium mucilage were incorporated in the tablet which was used as the check point of the regression analysis model (Tables 1 and 2).

### *Evaluation of Mixed Powder Blend of Drug and Excipients*

Evaluation of mixed blends of drug and excipients were carried out for all the formulations for angle of repose, bulk density, tapped density, Hausner's ratio and Carr's index.

#### *Bulk density ($D_b$) and tapped density ($D_t$)*

Both bulk density and tapped bulk density were determined. A suitable amount of powder from each formulation, previously lightly shaken to break agglomerates formed, was introduced into a 10 ml measuring cylinder. After initial volume was observed, the cylinder was allowed to fall under its own weight on to a hard surface from a height of 2.5 cm at 2 seconds intervals. The tapping was continued until no further change in volume was noted. Bulk density and tapped bulk density were calculated

**Table 1.** Factorial design batches

| Ingredients | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ |
|---|---|---|---|---|---|---|---|---|---|
| **Rizatriptan benzoate** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Crospovidone** | 3 | 6 | 9 | 3 | 6 | 9 | 3 | 6 | 9 |
| **Psyllium mucilage** | 6 | 6 | 6 | 9 | 9 | 9 | 12 | 12 | 12 |
| **Aerosil** | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| **Magnesium stearate** | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| **Aspartame** | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| **Avicel PH 102 up to** | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |

F: formulation

**Table 2.** Design and summary response data

| Run | Independent variable in code form | | | | Dependent variable | | |
|---|---|---|---|---|---|---|---|
| | Coded form | | Actual form | | | | |
| | **Factor A** | **Factor B** | **Psyllium mucilage** (mg) | **C.P** (mg) | **WT** (S) | **DT** (s) | $Q_5$ % |
| 1 | -1 | -1 | 6 | 3 | 62 | 56 | 84 |
| 2 | -1 | 0 | 6 | 6 | 59 | 54 | 93 |
| 3 | -1 | 1 | 6 | 9 | 51 | 48 | 100 |
| 4 | 0 | -1 | 9 | 3 | 49 | 45 | 90 |
| 5 | 0 | 0 | 9 | 6 | 44 | 41 | 97 |
| 6 | 0 | 1 | 9 | 9 | 41 | 37 | 101 |
| 7 | 1 | -1 | 12 | 3 | 40 | 32 | 84 |
| 8 | 1 | 0 | 12 | 6 | 30 | 27 | 83 |
| 9 | 1 | 1 | 12 | 9 | 33 | 30 | 81 |

C.P: crospovidone, WT: Wetting time, DT: Disintegration time, $Q_5$: Drug release after 5 minutes

using following formula (13):

$$D_b = \frac{weight\ of\ the\ power}{volume\ of\ the\ packing}$$

$$D_t = \frac{weight\ of\ the\ power}{tapped\ volume\ of\ the\ packing}$$

### *Carr's index*

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a Simple test to evaluate the $D_b$ and $D_t$ of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

$$Carr\ index = \frac{D_t - D_b}{D_t} \times 100$$

Where $D_t$ is tapped density of the powder and $D_b$ is bulk density of the powder.

### *Hausner's ratio*

Hausner's ratio was calculated from bulk and tapped density of Rizatriptan blend powder formulation and it is expressed as:

$$Hausner's\ ratio = \frac{D_t}{D_t}$$

Where $D_t$ is tapped density and $D_b$ is bulk density.

### *Angle of repose*

Angle of repose (θ) was determined using fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the granular cone was measured and angle of repose was calculated using the following equation:

$$\tan\theta = \frac{h}{r}$$

Where *h* and *r* are the height and radius of the cone (Table 3).

## *Evaluation parameters of orally disintegrating tablets*

### *Weight variation*

Randomly, 20 tablets were selected after compression and the mean weight was determined (14). None of the tablets deviated from the average weight by more than ±7.5%.

**Table 3.** Powder flow properties of the Rizatriptan formulations

| Code | Angle of repose (θ) | Bulk density (gr/cm$^3$) | Tapped density (gr/cm$^3$) | Carr's index (I) | Hausner's ratio |
|---|---|---|---|---|---|
| $F_1$ | 31.4±0.02 | 0.37±0.06 | 0.41±0.02 | 10.15±1.13 | 1.11 |
| $F_2$ | 31±0.03 | 0.32±0.07 | 0.35±0.02 | 09.10±1.01 | 1.10 |
| $F_3$ | 30.6±0.02 | 0.34±0.04 | 0.37±0.02 | 07.94±0.35 | 1.08 |
| $F_4$ | 30.1±.003 | 0.36±0.02 | 0.39±0.02 | 06.63±1.27 | 1.07 |
| $F_5$ | 30.3±0.01 | 0.33±0.03 | 0.36±0.02 | 09.53±1.05 | 1.10 |
| $F_6$ | 29.4±0.05 | 0.35±0.04 | 0.39±0.01 | 09.53±1.11 | 1,10 |
| $F_7$ | 29±0.02 | 0.36±0.07 | 0.39±0.01 | 07.08±1.36 | 1.07 |
| $F_8$ | 29.4±0.01 | 0.37±0.05 | 0.43±0.01 | 14.75±1.55 | 1.17 |
| $F_9$ | 28.9±0.03 | 0.34±0.07 | 0.37±0.02 | 07.94±0.35 | 1.08 |

F: formulation

### *Tablet thickness*

The thickness was measured by placing tablet between two arms of the Vernier calipers. 5 tablets were taken and their thickness was measured (15).

### *Tablet hardness*

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The hardness of the tablets was determined by diametral compression using erweka Hardness Tester (16).

### *Friability Testing*

This test was performed to determine the effects of friction and shock. Pre-weighed sample of 10 tablets was placed in the erweka friabilator and rotated at 25 rpm for about 4 min. The tablets were dedusted and reweighed, and the friability percentage was calculated. Compressed tablets should not lose more than 1% of weight (17).

$$Percentage\ friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

### *Wetting time*

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10-cm diameter were placed in a petridish with a 10-cm diameter. Ten milliliters of water containing eosin, a water-soluble dye, was added to the petridish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. The wetting times were measured (18)

### *Water absorption ratio*

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation (19).

$$R = \frac{W_a - W_b}{W_a} \times 100$$

Where, $W_b$ is the weight of the tablet before water absorption and $W_a$ is the weight of the tablet after water absorption.

### *In vitro disintegration test*

The in vitro disintegration studies were carried out using a Digital Tablet Disintegration test Apparatus (Erweka ZT- Germany). One tablet was placed in each of the six tubes of the basket assembly and then disk was added to each tube. This assembly was then suspended in a one-liter beaker containing water with its temperature being maintained at 37±2 °C. The basket was then moved up and down through a distance of 5 to 6 cm, at the frequency of 28 to 32 cycles per minute. The time required for complete disintegration of the tablet was recorded (20).

### *Dissolution test*

The release rate of Rizatriptan benzoate from orally disintegrating tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl pH 1.2 as a dissolution medium, at 37±0.5 °C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 10, 20 and 30 min. The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 280 nm using a Shimadzu spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve (21).

### *Content uniformity*

Ten tablets of each batch were weighed and powdered. Aliquot of this powder containing Rizatriptan benzoate equivalent to 5 mg of Rizatriptan was accurately weighed, suspended in approximately 50 ml of 0.1 N HCl and shaken for 15 min. Final volume was adjusted to 100 ml with 0.1 N HCl and filtered (Whatmann No.1 filter paper). From this 10 ml was diluted to 100 ml. The final volume was made by taking 2 ml of above solution and diluted to

**Table 4.** Evaluation of the prepared orodispersible tablets of Rizatriptan

| Tests | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ |
|---|---|---|---|---|---|---|---|---|---|
| Weight variation (Mean±SD) | 151±3.45 | 149±2.24 | 149±3.12 | 150±3.71 | 152±3.32 | 148±1.58 | 147±3.28 | 151±3.45 | 149±2.24 |
| Hardness (kg/cm²) | 3.81±0.25 | 3±0.27 | 3.8±0.22 | 3.8±.023 | 3.7±0.27 | 3.1±0.19 | 3.7±0.22 | 3±0.23 | 3.2±0.21 |
| Friability | 0.57±0.16 | 0.68±0.14 | 0.81±0.15 | 0.93±0.147 | 0.96±0.157 | 0.72±0.155 | 0.44±0.138 | 0.80±0.149 | 0.66±0.153 |
| Thickness (mm) | 3.2 | 2.9 | 3.00 | 3.1 | 3.1 | 3.2 | 2.9 | 3.3 | 3.4 |
| Wetting time (s) | 62 | 59 | 51 | 49 | 44 | 41 | 40 | 30 | 33 |
| Water absorption ratio | 78.12 | 80.25 | 82.34 | 85.74 | 86.64 | 88.57 | 90.47 | 93 | 91 |
| In-vitro disintegration time (s) | 56 | 54 | 48 | 45 | 41 | 37 | 32 | 27 | 30 |
| Assay | 98.3 | 97.2 | 98.7 | 96.7 | 98.2 | 95.8 | 99.4 | 97.2 | 97.3 |

F: formulation

10 ml with 0.1 N HCl. Absorbance of this solution was recorded at 280 nm using UV/Vis spectrophotometer against a reagent blank and the content was compared from a calibration curve prepared with standard Rizatriptan benzoate in the same medium (Table 4). The mean percent drug content was calculated as an average of three determinations (22).

### *Data analysis*

Response surface model factorial designs with 2 independent formulation variables at 3 different levels were used to study the effect of dependent variables (23). All the batches of orally disintegration were statically (95% or $p<0.05$) evaluated with regard to disintegration time, wetting time and drug release after 5 minutes.

### *Optimization of formulation ingredients*

After generating the polynomial equations relating the dependent and independent variables, the process was optimized for responses, optimization was performed to obtain the value of $X_1$ and $X_2$, which targeted disintegration time (DT)= 35 seconds; wetting time (WT)= 40 seconds; drug release after 5 minutes ($Q_5$) =99. The optimized amount of crospovidone and Psyllium mucilage was incorporated in the tablet which was also used as the check point of the regression analysis model (24). The optimized orally disintegrating tablet was prepared and evaluated for the physiochemical properties.

## Results

### *Data analysis*

A response surface model factorial design with 2 independents variable at 3 different levels was used to study the effects in dependent variables. All the batches if orally disintegrating time, wetting time and drug release after 5 minutes. Transformed values of the batches along their results are show in Table 5. the dependent variables (DT,WT, $Q_5$) obtained at various levels of the 2 independent variable ($X_1$ and $X_2$) were subjected to multiple regressions to yield a second-order polynomial equation, the obtained coefficient are shown in Table 5. The DT, WT and $Q_5$ values measured form different batches shows wide variation. These results clearly indicated the DT, WT and $Q_5$ are strong affected by the variables selected for the study. This was also reflected by the wide range of value for coefficients of the term equation the value of correlation coefficient ($R^2$) of polynomial regression equation was found to be greater than 0.99, indication good fit for all dependent variable shown in Table 5.

$X_1$ and $X_2$ represents the average result if changing one variable at a time from its low level to its high level. The interaction terms ($X_1X_2$, $X_1X_1$ and $X_2X_2$) show how the DT, Wt and $Q_5$ changes when 2 variables are simultaneously changed. Using the polynomial equations, the optimized formulations were obtained for the response parameters.

### *Polynomial equation for disintegration time*

$$Y=43.56-14.5X_1-4X_2+1X_1X_2+1.17X_1^2+1.67X_2^2$$

### *Polynomial equation for wetting time*

$$Y=40.56-13.5X_1-4X_2+1.5X_1X_2+0.17X_1^2+0.67X_2^2$$

### *Polynomial equation for drug release after 5 minutes*

$$Y=96.67-5X_1+5.5X_2-4.75X_1X_2-8.5X_1^2+1X_2^2$$

### *Response surface counterplot*

The relationship between the dependent and independent variable was further elucidate by constructing counter plots. The effects of $X_1$ and $X_2$ with their interaction on DT, WT and $Q_5$ at different levels (low, medium and high level) are displayed in Figures 1-3 .the interaction effect between $X_1$ and $X_2$ are shown in response surface plot Figures 4-6.

### *Optimization of orally disintegrating tablet*

The optimization of the orally disintegrating tablet was decided to target DT= 35 sec, WT= 40 and drug release $Q_5$= 99%.

Optimized concentrations were obtained from the software and the counter plot shown in Figure 7. Comparative values of predicted and observed responses along with the

**Table 5.** Analysis of variance (ANOVA) response surface cubic model

| | Source | Sum of squares | Df | Mean square | F value | Prob of P value< F value | $R^2$ |
|---|---|---|---|---|---|---|---|
| For Wetting time | Model | 945.78 | 7 | 135.11 | 304.00 | 0.0441 | 0.9995 |
| | $X_1$ | 420.50 | 1 | 420.50 | 946.13 | 0.0207 | |
| | $X_2$ | 32.00 | 1 | 32.00 | 72.00 | 0.0747 | |
| | $X_1X_2$ | 4.00 | 1 | 4.00 | 9.00 | 0.2048 | |
| | $X_1^2$ | 2.72 | 1 | 2.72 | 6.12 | 0.2445 | |
| | $X_2^2$ | 5.56 | 1 | 5.56 | 12.50 | 0.1755 | |
| | Residual | 0.44 | 1 | 0.44 | | | |
| | Cor total | 946.22 | 8 | | | | |
| For Disintegration time | Model | 872.44 | 7 | 124.63 | 280.43 | 0.0459 | 0.9995 |
| | $X_1$ | 364.50 | 1 | 364.50 | 820.13 | 0.0222 | |
| | $X_2$ | 32.00 | 1 | 32.00 | 72.00 | 0.0747 | |
| | $X_1X_2$ | 9.00 | 1 | 9.00 | 20.25 | 0.1392 | |
| | $X_1^2$ | 0.00 | 1 | 0.00 | 0.12 | 0.7837 | |
| | $X_2^2$ | 0.00 | 1 | 0.00 | 2.00 | 0.3918 | |
| | Residual | 0.44 | 1 | 0.44 | | | |
| | Cor total | 872.89 | 8 | | | | |
| For Drug release after 5 minutes | Model | 479.75 | 7 | 68.54 | 274.14 | 0.0465 | 0.9995 |
| | $X_1$ | 50.00 | 1 | 50.00 | 200.00 | 0.0449 | |
| | $X_2$ | 60.50 | 1 | 84.50 | 760.50 | 0.0231 | |
| | $X_1X_2$ | 90.25 | 1 | 90.25 | 361.00 | 0.0335 | |
| | $X_1^2$ | 144.50 | 1 | 144.50 | 578.00 | 0.0265 | |
| | $X_2^2$ | 2.00 | 1 | 2.00 | 8.00 | 0.2163 | |
| | Residual | 0.25 | 1 | 0.25 | | | |
| | Cor total | 480.00 | 8 | | | | |

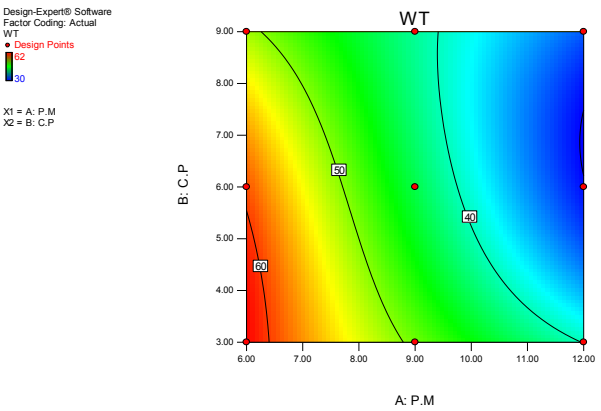


**Figure 1.** Counter plot for wetting time. WT: Wetting time, X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage.

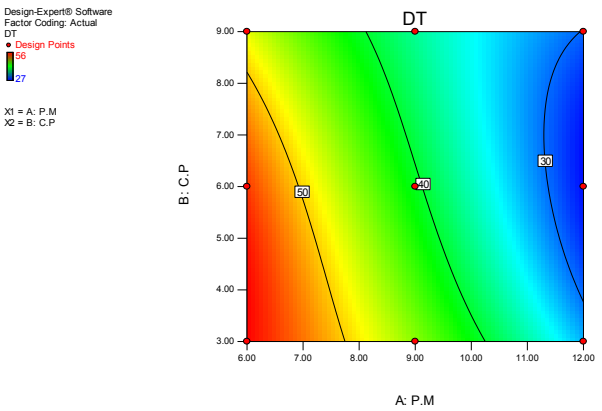


**Figure 2.** Counter plot for disintegration time. X1=A: P.M, X2=B:C.P; C.P: crospovidone, P.M: Psyllium mucilage, DT: disintegration time.

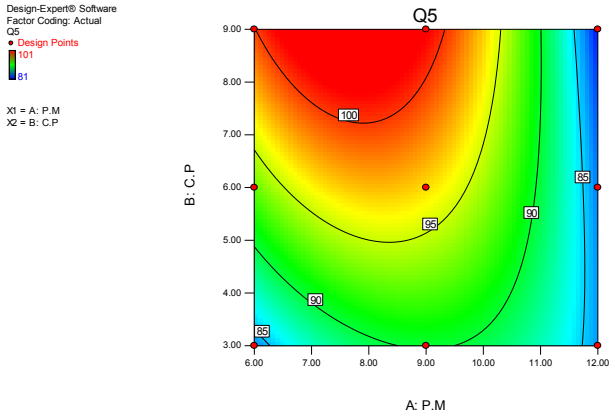


**Figure 3.** Counter plot for $Q_5$. X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage, $Q_5$: drug release after 5 minutes.

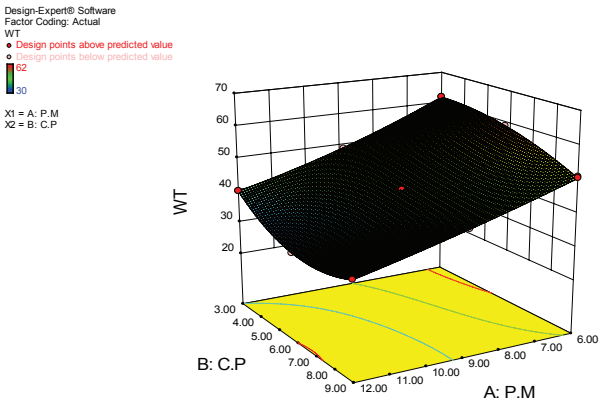


**Figure 4.** Response surface plot for wetting time. WT: Wetting time,X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage.

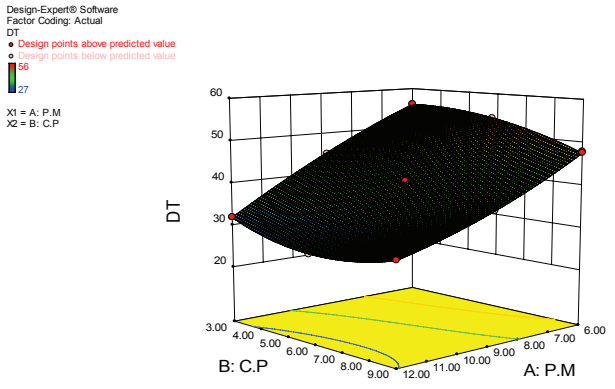


**Figure 5.** Response surface plot for Disintegration time. DT: Disintegration time, X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage.

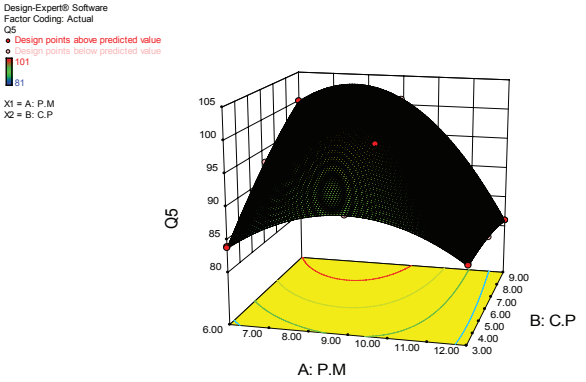


**Figure 6.** Response surface plot for $Q_5$. X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage, $Q_5$: drug release after 5 minutes.

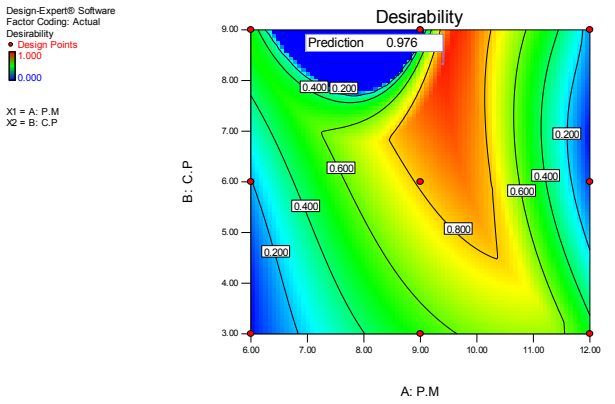


**Figure 7.** Counter plot for desirability. X1=A: P.M, X2=B:C.P, C.P: crospovidone, P.M: Psyllium mucilage.

formulation components are reported in Table 6.

## Discussion

An optimized formulation of Rizatriptan orally disintegrating tablet was prepared in this study using the "Direct compression" method. Formulation and optimization procedures were facilitated using $3^2$ full factorial designs.

About the WT and DT tests, it was observed that with increasing crospovidone and Psyllium mucilage DT and WT was both decreased; however, changes in the quantities of Psyllium mucilage had more significant effect than crospovidone (10).

On the other hand with increasing the percentage of Psyllium mucilage, speed of drug release was decreased, hence to create a suitable response, an optimum limit in usage Psyllium mucilage was found to have a proper amount of drug release.

**Table 6.** Comparative value of predicted and observed responses.

| $F_{NO}$ | Psyllium mucilage (mg) | crospovidone (mg) | DT (Sec) | | WT | | $Q_5$ | | Desirability |
|---|---|---|---|---|---|---|---|---|---|
| | | | Predicted | Observed | Predicted | Observed | Predicted | Observed | |
| $O_1$ | 9.40 | 8.32 | 36.47 | 36.3 | 39.99 | 39.2 | 99.00 | 99.12 | 0.976 |

WT: Wetting time, DT: Disintegration time, Q5: drug release after 5 minutes, O: Optimized batch

### *Effect of formulation vaiable on WT*

Value of prob>f less than 0.05 show the model for WT is significant and Factor $X_1$ is found to be significant in this case. The negative coefficient for $X_1$ and $X_2$ indicate favorable effect on WT [increasing the amount of C.P and P.M (Psyllium mucilage) decrease the WT]. The results convey us that factor $X_1$ has significant effect on WT than that of $X_2$.

### *Effect of formulation vaiable on DT*

Value of prob>f less than 0.05 show the model terms are significant and Factor $X_1$ is found to be significant in this case The negative coefficient for $X_1$ and $X_2$ indicate favorable effect on DT (increasing the amount of C.P and P.M decrease the DT). The results convey us that factor $X_1$ has significant effect on DT than that of $X_2$.

### *Effect of formulation vaiable on $Q_5$*

Value of prob>f less than 0.05 show the model for $Q_5$ is significant and factor $X_1$, $X_2$, and $X_1X_2$ and $X_1^2$ are significant. The positive coefficient for $X_2$ indicates favorable effect on WT (increasing the amount of C.P increase the $Q_5$). The results convey us that factor $X_2$ has significant effect on $Q_5$ than that of $X_1$.

## Conclusion

Overall, the results convey us that optimized orally disintegrating tablets of Rizatriptan containing 9.4 mg of C.P and 8.32 mg of P.M as a superdisntegrant by direct compression method showed responses as we desired.

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## Authors' contributions

All contributed in the study, MT, MAS and ESh prepared the manuscript and Mk edited it.

## Conflict of interests

The authors declared no competing interests.

## Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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