

# Statistical Designing and Characterization of Valsartan Oral Disintegrating Tablet

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**Abstract** The present study involves the formulation and characterization of valsartan (VT) oral disintegrating tablets by using crospovidone (CP) and *Hibiscus rosasinensis* (HRS) mucilage as complexing agent. Valsartan (VT), anti-hypertensive drug (class II) is an orally active non-peptide triazole-derived antagonist of angiotensin II. The direct compression method was used to obtain 13 such formulations, and the tablets obtained were evaluated for drug content, hardness, friability (FT), disintegration time (DT) and dissolution rate. A significant increase in the dissolution rate of VT was obtained. FTIR and DSC studies showed no interaction between the drug and excipients. The amount of CP ( $X_1$ ) and amount to HRS mucilage ( $X_2$ ) is selected for  $3^2$  factorial designs. The DT ( $Y_1$ ), FT ( $Y_2$ ) and % drug released at 25 min ( $Y_3$ ) interval were taken as the response variables.  $X_1$  and  $X_2$  represents the result of changing the variable at a time from low level to high level. The interaction terms ( $X_1X_2$ ,  $X_1^2$ ,  $X_2^2$ ,  $X_1^2X_2$  and  $X_1X_2^2$ ) exhibited that  $Y_1$ ,  $Y_2$  and  $Y_3$  had changed simultaneously (as analyzed by Design expert software 8 version). The contour and 3D plots revealed that there is an effect of  $X_1$  and  $X_2$  with the interaction on  $Y_1$ ,  $Y_2$  and  $Y_3$ .  $F_2$  formulation exhibited minimum errors with CP and HRS in response to dependable variables which is concluded as best formulation.

**Keywords** Valsartan, *Hibiscus rosasinensis*, Optimization, Oral Disintegrating Tablets

## 1. Introduction

New technologies are revolutionizing the drug discovery and the novel formulation development in pharmaceutical industries. In this regard, novel concepts of drug delivery systems have much therapeutic benefit, which may improve the efficacy and duration of drug activity. Moreover, such systems increase the patient compliance by reducing the dosing frequency, provide easy routes of drug administration and improve site-specific drug delivery to reduce adverse effects [1,2].

Nearly, 95% of new active pharmaceutical ingredient drug demonstrates low and variable oral bioavailability due to their poor aqueous solubility at physiological pH, resulting in a lower dissolution rate. The drug which shows low solubility and high permeability come under class II according to Biopharmaceutics Classification System (BCS). Hence, it has been a tough challenge for the pharmaceutical scientists to formulate oral disintegrating tablet for poorly soluble drugs as it requires enhancement in the dissolution rates [3-5]. The techniques that have been generally employed for enhancing the solubility of drugs include micronisation and cyclodextrin-complexation which involves the use of surfactants, solubilizers and super disintegrants. They

improve the solubility of class-II drugs by increasing the dissolution rate and bioavailability significantly [6]. Nevertheless, complexation with cyclodextrin and using super disintegrants such as crospovidone and sodium starch glycolate are industrial methods that are largely used to enhance the dissolution rate of poorly soluble drugs during the formulation development. The super disintegrants are added to facilitate drug release and improve the dissolution rate [7-9].

*Hibiscus rosasinensis* mucilage acts as a super disintegrant. It is chemically composed of cyclopropanoids, methyl stercolate, methyl-2-hydroxyl stercolate, 2-hydroxyl stercolate malvate and  $\beta$ -rosasterol. Its leaf contains carotene, protein, fat, carbohydrate, fibers, calcium and phosphorus, while the mucilage constitutes L-rhamnose, D-galactose, D-galactouronic acid and D-glucuronic acid [10,11]. Moreover, crospovidone (crosslinked polyvinyl N-pyrrolidone) is used in combination with active ingredients in medications and dietary supplements for allowing the absorption of active drug [12].

Response surface methodology is a widely employed technique that is used for formulating and optimizing drug formulation with suitable experimental design [13]. Valsartan is widely prescribed anti-hypertensive drug that possesses poor aqueous solubility and low dissolution rate [14]. Hence, this study investigates the formulation and optimization of valsartan as oral disintegrating tablets by crospovidone and *hibiscus rosasinensis* mucilage as complexing agent by response surface methodology technique.

## 2. Materials and Methods

### 2.1. Materials

Valsartan was obtained from Hetero Drugs Private Limited, India. *Hibiscus rosasinensis* mucilage and crospovidone were procured from Natco Pharma Limited, India. Free trial version 8 Design expert software was used in statistical designing of drugs. All reagents were prepared in double distilled water with chemicals of analytical grade.

### 2.2. Extraction of HRS Mucilage

The matured leaves of HRS were collected, followed by washing and drying at 37 °C for 1 day. They were then crushed and soaked in warm water for 2-3 h and heated at 80-90 °C for 30-45 min. The mixture obtained was kept for 1 day in order to bring out the complete release of water soluble mucilage (i.e. polysaccharide) into the solvent. The mucilage was then extracted by using a cheese cloth bag to remove the mark for obtaining a concentrated viscous solution. Acetone was added to the

concentrated viscous solution with constant stirring. The gel like precipitate was formed and then separated by filtration. The precipitate was washed thrice with acetone. The resulting precipitate was dried in oven at 40±1 °C followed by air drying overnight. The compact mass was collected, grounded, passed through a sieve #50 and stored in a desiccator until further use. The dry powder was considered as water soluble polysaccharide mucilage for pharmaceutical use [11].

### 2.3. Formulation of Valsartan Tablets

The optimization of Valsartan tablets was performed according to 3<sup>2</sup> factorial design. It includes crospovidone (CP) as 2.5%, 5% and 7.5% and *Hibiscus rosasinensis* (HRS) mucilage as 5%, 10% and 15% of the total weight of the tablet, and are considered as independent variables and dependent variables, respectively. Disintegration time (DT), Friability (%) and Cumulative Drug Release (%) at 25 min were dependent variables. Other excipient includes magnesium stearate (2 mg), aerosil (2 mg), talc (2 mg) and flavor (6 mg). Nine tablet formulations were prepared by a direct compression technique. The weight of tablet was 200 mg with 50 tablets batch size (Table 1).

### 2.4. Experimental Design

The amount of crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) were selected as independent variables, and were studied at 3 levels each. The central point was performed in triplicates. All other formulations and processing variables were kept invariant throughout the study. 13 experimental runs were made in the study (Table 1 and Table 2). Their factor combination and translation of the coded level to the experimental units were employed during the study. Disintegration time ( $Y_1$ ), friability ( $Y_2$ ) and cumulative drug released at 25 minutes ( $Y_3$ ) was taken as response variables.

### 2.5. Evaluation of the Oral Disintegrating Tablets (ODT)

10 tablets from each formulation were taken for measurement of diameter and crown thickness with Vernier caliper, and an average of ten determinations was carried out. Hardness of the prepared oral disintegrating tablets (ODT) was evaluated by using hardness tester. Weight variation test was performed for 20 tablets from each batch and average values were calculated. Friability of the prepared ODT was determined by weighing 10 tablets, and placing in a friability tester (Roche friabilator, Pharma Labs, Ahmedabad, India), which was rotated for 4 min at 25 rpm. After the de-dusting, the weight of the tablets was recorded and the % friability was calculated. Disintegration test was performed for the prepared ODT by using single unit disintegration test apparatus

(Paramount) by employing phosphate buffer (pH 6.8) as test fluid. The disintegration time was noted for all the formulations. The drug content uniformity was also performed by crushing ten ODT tablets in a glass mortar and pestle. An accurately weighed quantity of powder equivalent to 20 mg of valsartan was taken into 100 ml volumetric flask, dissolved in the assay buffer and the solution was filtered through Whatman filter paper no. 41. The filtrate was collected and suitably diluted with a phosphate buffer of pH 6.8 and assayed for valsartan at 250 nm. The flow properties such as angle of repose, bulk density tapped density, Hausner's ratio and Carr's index were also evaluated.

The wetting time and water absorption ratio were also evaluated for the prepared valsartan tablets. The measurement of wetting time was done by using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a petri dish with a 10 cm diameter. About 10 mm of water containing a water-soluble dye was added to the petri dish. At room temperature, F<sub>2</sub> formulation tablets were kept carefully on the surface of tissue paper in a petri dish. Time taken by water molecules to reach the upper surface of the F<sub>2</sub> formulation until measured it gets wet completely. The analysis was carried out ( $n = 20$ ), and the mean value was calculated.

The water absorption ratio,  $R$ , was determined according to the following equation:

$$R = 100(W_a - W_b)/W_a$$

Where,  $W_a$  and  $W_b$  are the weight before and after water absorption, respectively.

## 2.6. In-vitro Drug Release Studies

*In vitro* dissolution studies, the prepared ODT were conducted for a period of 25 min using six station USP XXII type 2 apparatus (Lab India Disso 2000 system, India) at  $37 \pm 0.5^\circ\text{C}$  at 50 rpm. The dissolution studies were carried out in triplicate for 25 min in 900 ml potassium phosphate buffer (pH 6.8) at different time intervals. Sample (5 ml) was withdrawn with a pre-filter and replaced with the same buffer to maintain sink conditions. After suitable dilution, samples were analyzed at 250 nm using UV spectrophotometer (SL-150, Elico, India). The amount of drug presented in the samples was calculated with the help of appropriate calibration curves constructed from reference standards. The physical changes of the formulations were observed throughout the drug release studies.

## 2.7. Characterization of Release Data

The description of dissolution profiles was attempted using different release models [15-16]. The data was evaluated according to the following equations:-

Zero order:

$$Mt = M_0 + K_0t$$

First order:  $\ln Mt = \ln M_0 + K_1t$

Where  $M_t$  is the amount of drug dissolved in time  $t$ ,  $M_0$  is the initial amount of drug,  $K_1$  is the first order release constant and  $K_0$  is the zero-order release constant.

## 2.8. FTIR Study

FTIR spectra (FTIR Spectrum RX1, Perkin Elmer Ltd, Switzerland) were obtained by scanning the sample in KBr discs. The samples of pure valsartan and ODT tablets were scanned individually.

## 2.9. DSC Study

DSC scan was performed for the pure drug valsartan and the ODT tablets F<sub>2</sub> by DSC-827e, Mettler, Toledo-Inc, 1900, USA. The aluminum pans were used in the experiment and the empty pan were also sealed to be used as references. The temperature was calibrated with indium as standard. The scanning rate of samples was from 50-300 °C at 10 °C/min.

## 3. Results and Discussion

The current study reveals the optimization procedure of preparing a series of ODT tablet formulations for valsartan by varying the concentrations of formulation ingredients in a systematic manner. This procedure was simplified by applying factorial designs and fitting into an empirical polynomial equation to the experimental results. These formulations were then assessed for appearance, taste, hardness, dissolution rate and other stability studies. Based on these results, F<sub>2</sub> formulation was predicted to be optimal. The translation code for the prepared ODT has been shown in Table 1 and 2. The data for friability %, disintegration time and cumulative percentage drug release (response variable) is shown in Table 3. Moreover, Table 4 exhibited the composition of the optimized formulation of valsartan ODT, the predicted and experimental values of response variables. Valsartan tablets formulated by employing HRS mucilage weighed 21.25 mg (Table 5). F<sub>2</sub> formulation disintegrated within 16 sec and exhibited least friability data (Table 3). Table 6 depicts good flow properties for F<sub>2</sub> formulations, the post-compression parameters, and measured values of wetting time and water absorption ratio. Fig 7 also shows the dispersion and wetting time for F<sub>2</sub> formulation. The hardness of the tablets was in the range 3.5-4.5 kg/cm<sup>2</sup>. However, weight loss in the friability test was less than 0.75 % in all the cases. It should be noted that the valsartan content of the tablets prepared was within  $99.85 \pm 0.33$  %.

### 3.1. In-vitro Drug Release Studies

Drug release studies were carried out for 25 min in neutral pH buffer. The amount of valsartan released from the ODT was observed and calculated. The percentage of drug released from all the designed formulations is shown in Table 5. Visual observations revealed that the tablets appeared swollen almost from the beginning. CP and HRS showed rapid hydration and forms loose channels for the passage of drug VT. The dissolution study revealed that all the tablets were completely eroded. It might be attributed to the formation of a very loose porous mass with CP and HRS in 1:3 ratio. This step leads to the initiation of drug VT to disperse readily and rapidly. Hence, the dissolution rate may be enhanced by complexation [1,12].

### 3.2. Characterization of Release Data

The dissolution mechanism was characterized by using different release models. The correlation co-efficient ( $r^2$ ) for zero order kinetics and first order kinetics were interpreted for all the formulations. The data proves that the VT tablets follow first order release kinetics with higher  $r^2$  values and rapid release of drug due to the presence of complexing of CP: HRS mucilage.

**Table 1.** Experimental Design carried out for ODT of Valsartan with CP and HRS

Formulation	Coded factor levels	
	X1	X2
F 1	-1	-1
F 2	0	-1
F 3	1	-1
F 4	-1	0
F 5	0	0
F 6	1	0
F 7	-1	1
F 8	0	1
F 9	1	1

**Table 2.** Translation of Coded levels in Actual units

Coded Level	-1	0	+1
<b>Independent variables</b>			
X1: Crospovidone (%)	2.5	5	7.5
X2: H. rosasinensis mucilage (%)	5	10	15
<b>Dependent variables</b>			
Y1	Disintegration time (sec)		
Y2	Friability (%)		
Y3	Cumulative Drug Released at 25 minutes (%)		

**Table 3.** Response Variables ( $Y_1$ ,  $Y_2$  and  $Y_3$ ) obtained from various Trial Formulations

Trial Run	Crospovidone (mg) ( $X_1$ )	H.R Mucilage (mg) ( $X_2$ )	Disintegration Time (sec) ( $Y_1$ )	Friability % ( $Y_2$ )	Cumulative % Drug Released % ( $Y_3$ )
F1	5	10	24±0.01	0.51±0.01	96.16±1.82
F2	10	10	16±0.04	0.45±0.02	97.02±2.37
F3	15	10	12±0.01	0.31±0.04	99.01±1.73
F4	5	20	15±0.02	0.37±0.05	96.50±1.54
F5	10	20	13±0.02	0.35±0.02	98.77±2.27
F6	15	20	10±0.01	0.25±0.01	99.81±1.55
F7	5	30	17±0.03	0.41±0.01	96.58±1.26
F8	10	30	19±0.01	0.49±0.02	96.16±2.89
F9	15	30	15±0.05	0.45±0.03	97.62±1.25

**Table 4.** Composition of the optimized formulation of valsartan ODT, the predicted and experimental values of response variables

No.	Crospovidone (mg)	H. rosasinensis Mucilage (mg)	Response Variables	Observed response	Predicted response	Percentage Error	Avg.
			Disintegration time	10.789	10.754	0.035	
F1	14.00	18.00	% Friability	0.244	0.255	-0.011	0.126
			Cumulative % drug released	99.362	99.695	-0.333	
			Disintegration time	10.575	10.66	-0.085	
F2	14.75	21.25	% Friability	0.266	0.255	0.011	0.116
			Cumulative % drug released	100.107	99.853	0.254	
			Disintegration time	10.772	10.637	0.135	
F3	14.28	15.58	% Friability	0.288	0.256	0.032	0.159
			Cumulative % drug released	99.391	99.702	-0.311	
			Disintegration time	10.365	10.646	-0.281	
F4	14.12	17.25	% Friability	0.285	0.252	0.033	0.253
			Cumulative % drug released	99.292	99.737	-0.445	
			Disintegration time	10.808	10.94	-0.132	
F5	14.75	12.75	% Friability	0.275	0.272	0.003	0.193
			Cumulative % drug released	99.144	99.485	-0.341	
			Disintegration time	10.92	10.998	-0.078	
F6	14.00	20.00	% Friability	0.293	0.262	0.031	0.154
			Cumulative % drug released	99.986	99.631	0.355	
			Disintegration time	10.552	10.777	-0.225	
F7	14.02	15.88	% Friability	0.291	0.26	0.031	0.231
			Cumulative % drug released	100.053	99.616	0.437	
			Disintegration time	11.081	10.86	0.221	
F8	14.64	21.63	% Friability	0.285	0.261	0.024	0.242
			Cumulative % drug released	99.337	99.755	-0.418	
			Disintegration time	11.091	10.96	0.222	
F9	14.68	21.73	% Friability	0.295	0.27	0.025	0.243
			Cumulative % drug released	99.98	99.66	-0.419	

**Table 5.** Optimized formulation of valsartan as ODT (F<sub>2</sub>)

Composition	Amount (mg)
Valsartan	80
Pearlitol SD 100	48
Crospovidone	14.75
Hibiscus rosasinensis mucilage	21.25
Sorbitol	20
Other excipients	12
Aspartame	4

### 3.3. Optimization of Valsartan ODT

The optimization of valsartan ODT formulation was performed by Design Expert Software 8 version. Response surface methodology was used for the development and optimization of ODT [17-19]. Different steps involved in it include experimental design,

regression analysis, constraint optimization and validation. Polynomial models including interaction and quadratic terms were generated for all the response variables using multiple linear regression analysis (MLRA) approach. The general form of the MLRA model is represented by the following equation:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 X_2 + \beta_4 X_1^2 + \beta_5 X_2^2 + \beta_6 X_1 X_2^2 + \beta_7 X_1^2 X_2$$

$\beta_0$  is the intercept representing the arithmetic average of all quantitative outcomes of 9 runs;  $\beta_1$  to  $\beta_7$  are the coefficients computed from the observed experimental response values of Y, and  $X_1$  and  $X_2$  are the coded levels of the independent variable(s). The terms  $X_1 X_2$  and  $X_i^2$  ( $i = 1$  to 2) represent the interaction and quadratic terms, respectively. Two dimensional contour plots and three-dimensional response surface plots were constructed (Fig 1 to 6). Mathematical relationships in the form of a polynomial equation for the measured response

disintegration time, % friability and cumulative % drug released at 25 minutes were taken as the response variables. The polynomial equation relating to the different response and the independent variable is given below [20]:

$$Y1 \text{ (Disintegration time)} = +13.52 - 2.50 * X_1 + 1.50 * X_2 + 2.50 * X_1 * X_2 - 0.81 * X_1^2 + 4.19 * X_2^2 - 2.50 * X_1^2 * X_2 - 1.00 * X_1 * X_2^2 \quad \text{Eq(1)}$$

$$Y2 \text{ (% Friability)} = +0.33 - 0.060 * X_1 + 0.020 * X_2 + 0.060 * X_1 * X_2 - 0.032 * X_1^2 + 0.13 * X_2^2 - 0.010 * X_1^2 * X_2 + 0.020 * X_1 * X_2^2 \quad \text{Eq(2)}$$

$$Y3 \text{ (Cumulative % drug released)} = +98.09 + 1.66 * X_1 - 0.43 * X_2 - 0.45 * X_1 * X_2 + 0.34 * X_1^2 - 1.22 * X_2^2 + 0.19 * X_1^2 * X_2 - 0.68 * X_1 * X_2^2 \quad \text{Eq(3)}$$

### 3.4. Two Dimensional Contour Plots and Three-Dimensional Response Surface Plots

Fig 1 and 2 showed the effect of crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on disintegration time (sec). It was observed that Y1 (disintegration time) decreases with the increase in concentrations of both independent variables; however, after a certain level of concentration, DT increases. It might be attributed to the network formation of wetted particles (with HRS mucilage) of the independent variables. Fig 3 and 4 showed the effect of crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on friability. It indicates that the friability decreases by increasing the concentrations of both independent variables. It is also observed that the friability is decreased by increasing the concentration of HRS mucilage. Fig 5 and 6 showed the effect of crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on cumulative % drug release in 25 min. It was observed that the percentage of drug release was increased by increasing the concentration of HRS mucilage.

### 3.5. Validation of Response Surface Methodology Results for Valsartan ODT Formulation

The formulations corresponding to these checkpoints were prepared and evaluated for various response properties. Subsequently, the resultant experimental data of response properties were quantitatively compared with that of their predicted values. Table 4 showed the predicted and experimental values.  $F_2$  formulation exhibited the predicted and experimental value of disintegration time, the percentage of friability and cumulative % drug release with least percentage error among all the formulations. Hence,  $F_2$  formulation was chosen as the optimized ODT of valsartan with CP and HRS mucilage.

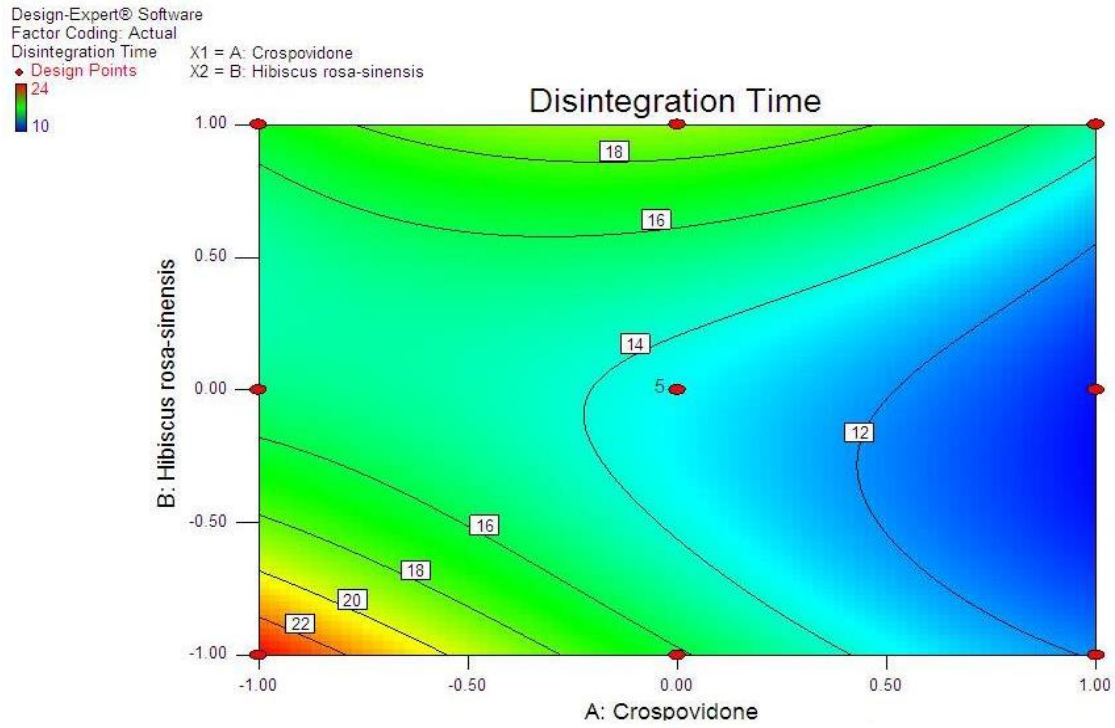
**Table 6.** Flow Properties and Post-compression parameters of the optimized formulation ( $F_2$ )

Properties	Optimized Formulation ( $F_2$ )
Angle of Repose ( $^\circ$ )	22.15
Bulk density	0.471
Tapped density	0.576
Carr's Compressibility Index	18.23
Hausner's Ratio	1.192
<b>Parameters</b>	<b>Value</b>
Wetting time (sec)**	8
Water Absorption ratio (%)**	91.11 $\pm$ 0.23
Weight variation (%) <sup>#</sup>	0.42
Hardness*	3.1 $\pm$ 0.37
Thickness(mm) *	3.1 $\pm$ 0.11
Content uniformity (%) <sup>#</sup>	99.81 $\pm$ 0.48
Average weight**(mg)	199.77

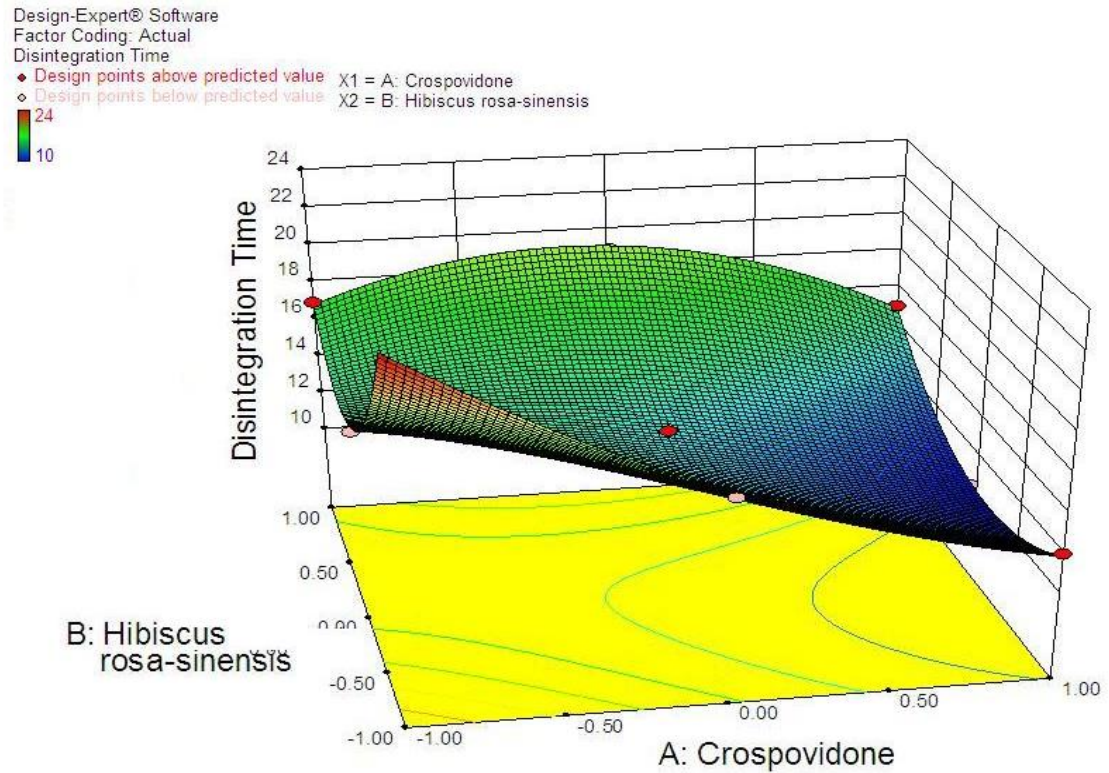
\*Each value was an average of six determinations

\*\*Each value was an average of three determinations

<sup>#</sup> Result of one batch, n=20



**Figure 1.** Contour plot showing the effect of crospovidone ( $X_1$ ) and HRS Mucilage ( $X_2$ ) on Disintegration time (sec)



**Figure 2.** Response surface plot showing the effect of Crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on Disintegration time (sec)

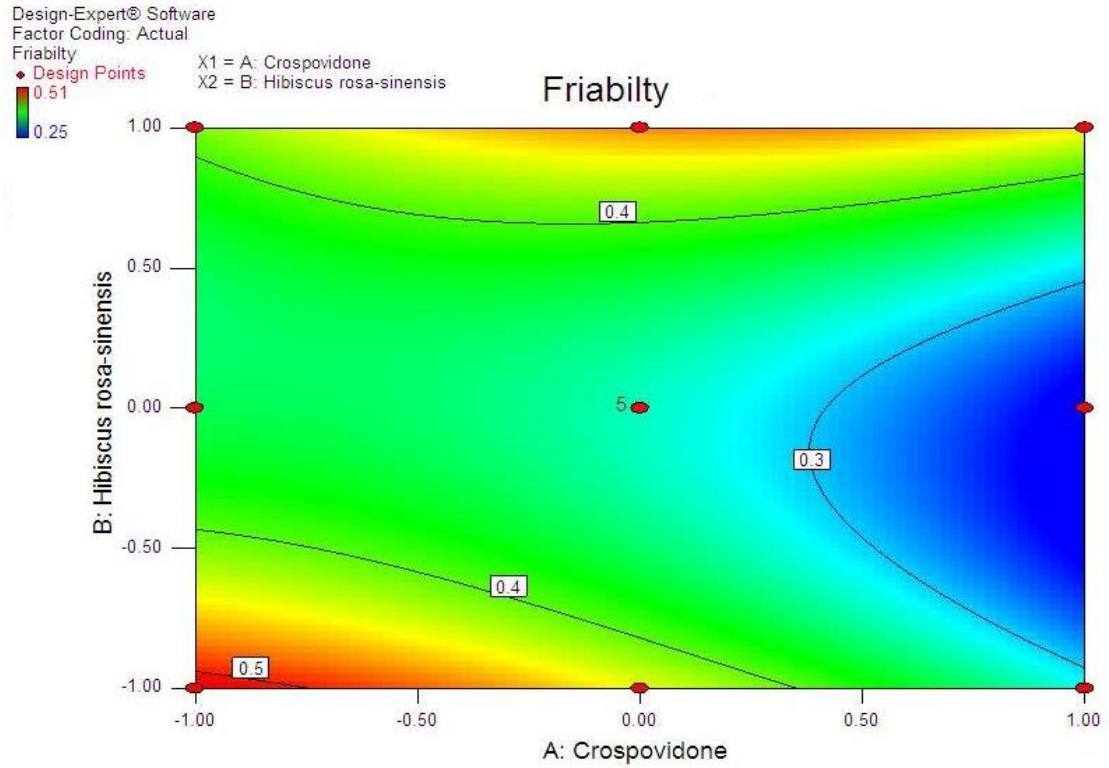


Figure 3. Contour plot showing the effect of Crospovidone (X<sub>1</sub>) and HRS mucilage (X<sub>2</sub>) on % Friability

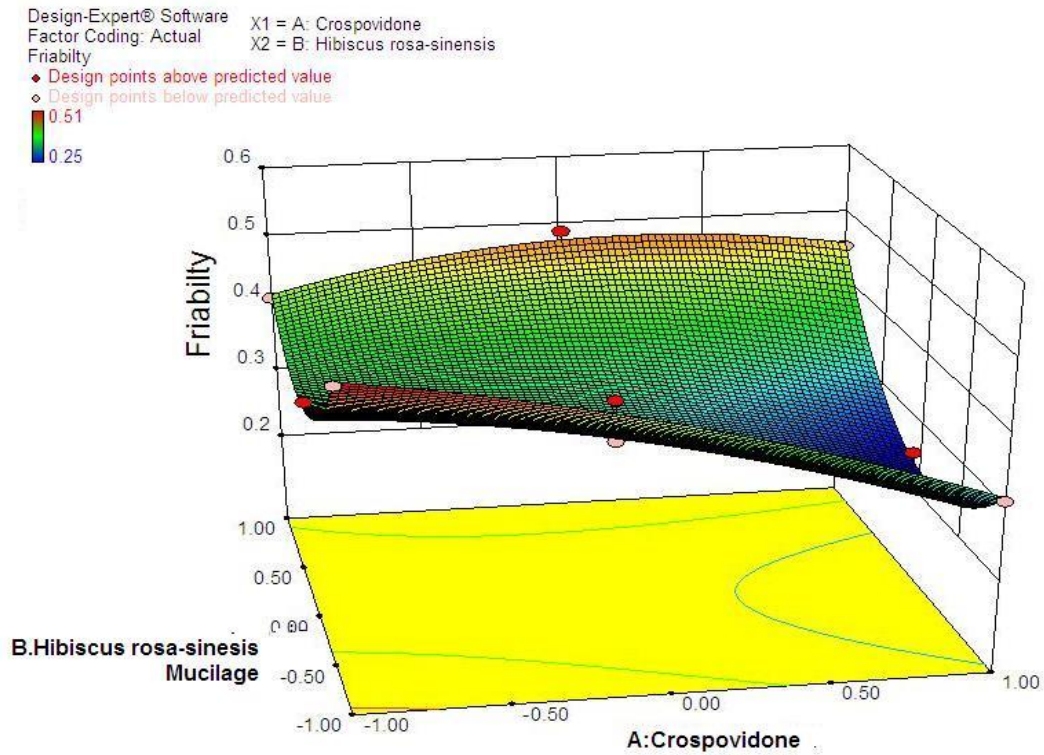


Figure 4. Response surface plot showing the effect of crospovidone (X<sub>1</sub>) and HRS mucilage (X<sub>2</sub>) on % Friability

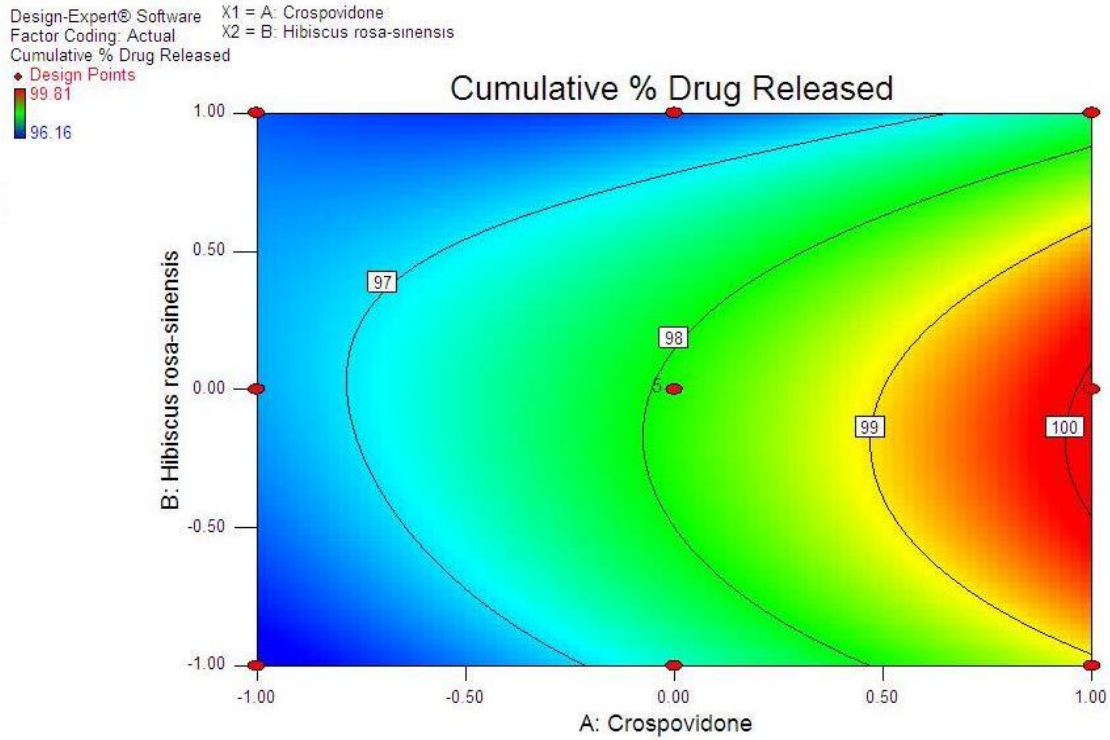


Figure 5. Contour Plot Showing Effect of Crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on % drug release in 25 min

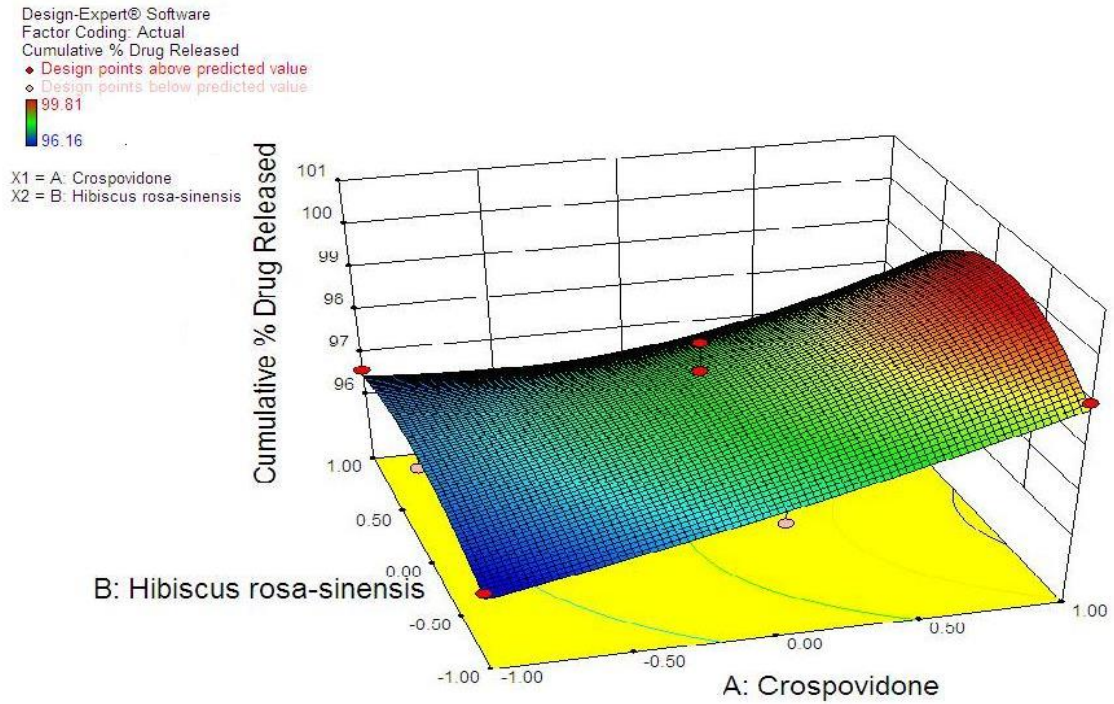
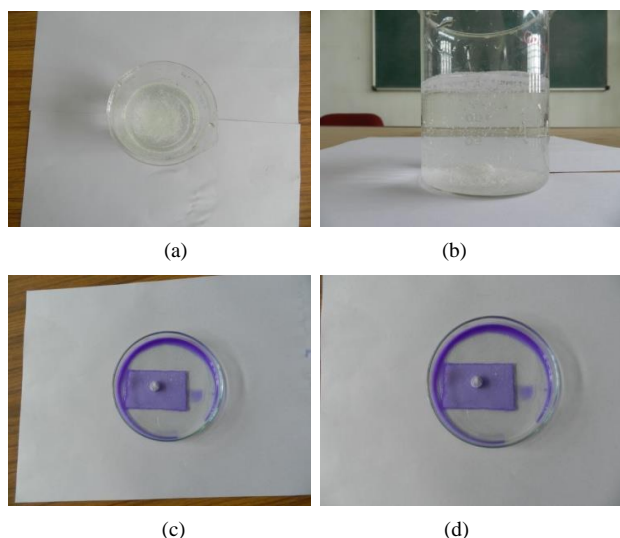


Figure 6. Response surface plot showing effect of Crospovidone ( $X_1$ ) and HRS mucilage ( $X_2$ ) on % drug released in 25 min



**Figure 7.** (a) Dispersion of formulation (F\*2) in 10.5 sec (Ariel view) (b) Dispersion of formulation (F\*2) in 10.5 sec (Side view) (c) Wetting time of formulation (F<sub>2</sub>) in 3 sec (d) Wetting time of formulation (F<sub>2</sub>) in 8 sec

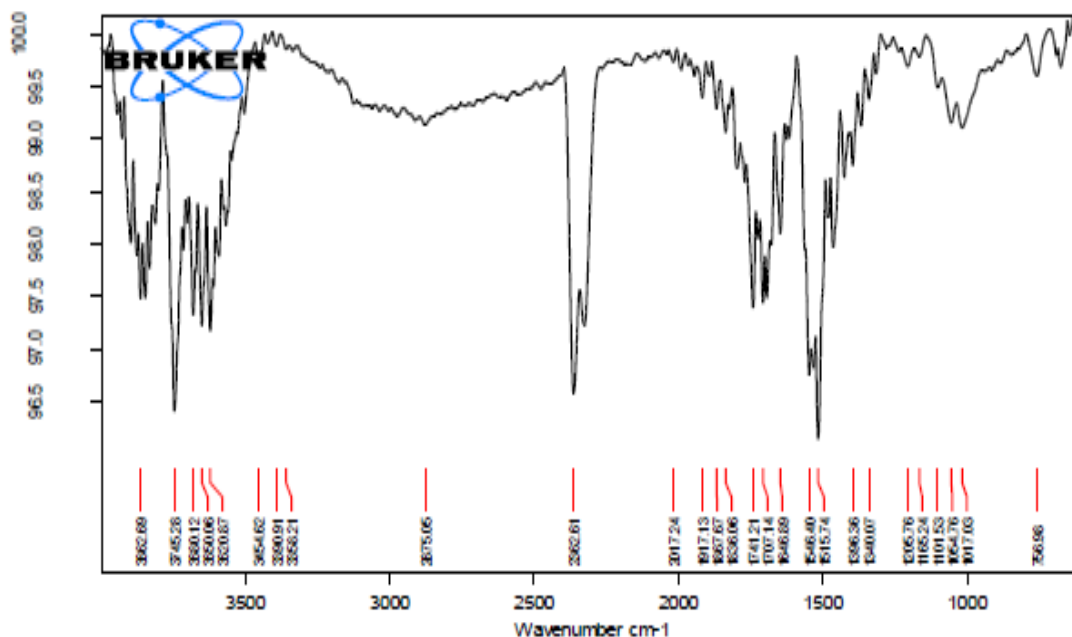
### 3.6. FTIR Studies

FTIR spectra revealed the presence of different functional groups in the compound (Fig 8). The characteristic absorption band was observed in 3610.28  $\text{cm}^{-1}$  (due to C-H stretching of alkane), 1198.26  $\text{cm}^{-1}$  and

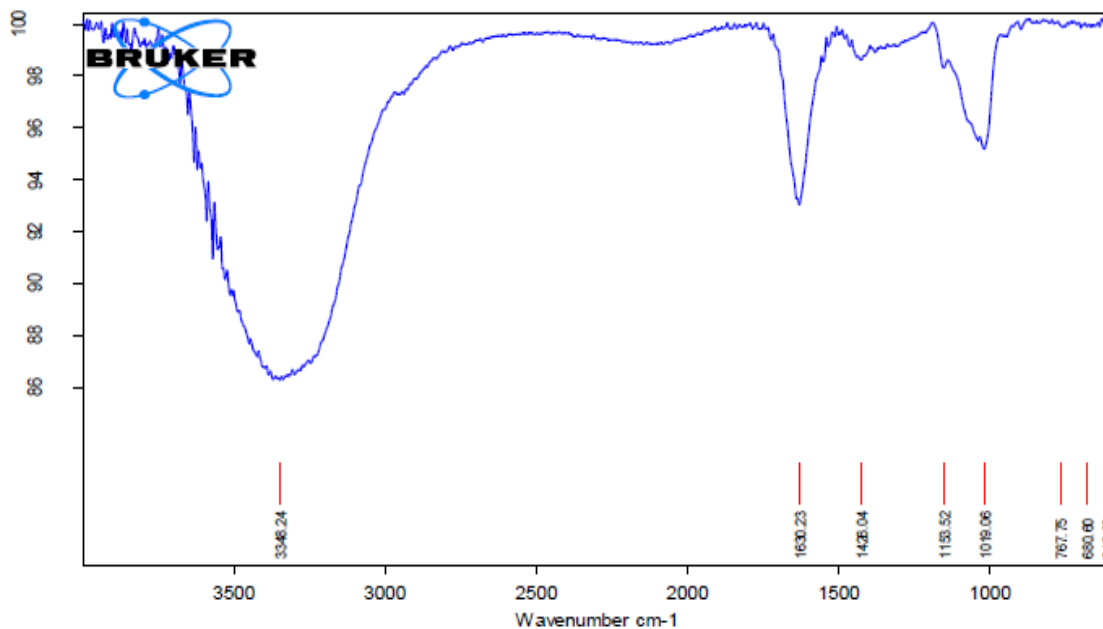
1019.96  $\text{cm}^{-1}$  (C-N vibration of aromatic tertiary amine), 1153.52  $\text{cm}^{-1}$  (due to C=O stretching of acyclic saturated) and 1426.59  $\text{cm}^{-1}$  (due to N-H group of aromatic secondary amine). The result suggested no chemical interaction between the drug and formulation which was confirmed due to disappearance of any characteristics peaks. The presence of peaks within the expected range confirmed that the materials utilized in drug formulation was unaffected thereby exhibiting no interactions.

### 3.7. DSC Studies

DSC thermogram for the pure drug valsartan exhibited sharp endotherm at 106.9  $^{\circ}\text{C}$  which corresponds to its melting point (Fig 9a). The melting endothermic peaks of valsartan in the formulation are almost nearer and these peaks are the strong evidences of inclusion of drug into HRS mucilage cavity. Hence, for the mucilage complex and the intensity of the valsartan (F2 formulation) melting endotherm peaks had decreased (102.1  $^{\circ}\text{C}$ ) as shown in Fig 8b and another peak at 179.35  $^{\circ}\text{C}$  which may be attributed to the presence of excipients in the physical mixture. The decreased and broadened peaks indicated complete amorphous state. These results concluded that interaction did not occur between the drug and excipients used in the study.

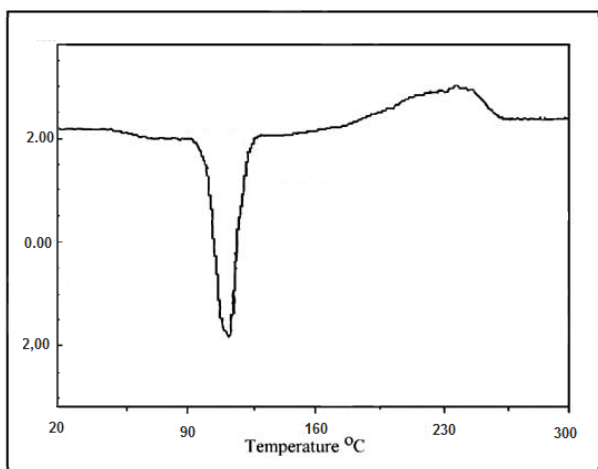


(A)

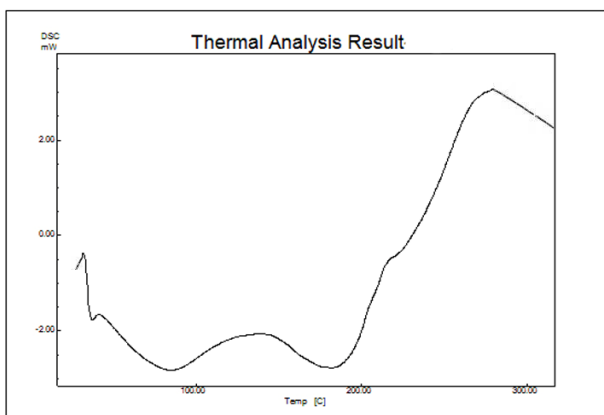


(B)

Figure 8. FTIR spectrum of valsartan pure (A) and optimized formulation F<sub>2</sub> (B)



A



B

Figure 9. DSC Thermogram of pure Valsartan (A) and formulation F<sub>2</sub> (B)

## 4. Conclusions

ODT of Valsartan was developed successfully by response surface methodology based on 3<sup>2</sup> factorial designs. Lower levels of CP and higher levels of HRS gave high disintegration time (Y<sub>1</sub>) with low friability % (Y<sub>2</sub>). It was also observed that there was an increase in the valsartan release with the combination of CP with HRS. F<sub>2</sub> formulation exhibiting minimum errors with CP and HRS in response to dependable variables was optimized as best formulation. FTIR and DSC studies show no interaction between the drug and the excipients.

## Abbreviations

VT: Valsartan  
 CP: Crospovidone  
 HRS: *Hibiscus rosasinensis*  
 ODT: Oral disintegrating tablets

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## Conflict of Interest

The authors declare no conflict of interest.

### Author Contributions

IAA: Basic ideas of the research, Application of data in Software and preparation of manuscript; CSP: Making HRS mucilage and different batch of tablets; SAA: Interpretation of the data generated from software and initial draft of the manuscript; AMA: Final draft of the manuscript and critical suggestion in revision stage.

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