ORIGINAL ARTICLE

Formulation and evaluation of fast dissolving tablets of cinnarizine using superdisintegrant blends and subliming material

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ABSTRACT

The aim of this investigation was to develop fast dissolving tablet of cinnarizine. A combination of super disintegrants, i.e., sodium starch glycolate (SSG) and crosscarmellose sodium (CCS) were used along with camphor as a subliming material. An optimized concentration of camphor was added to aid the porosity of the tablet. A 3^2 full factorial design was applied to investigate the combined effect of two formulation variables: Amount of SSG and CCS. Infrared (IR) spectroscopy was performed to identify the physicochemical interaction between drug and polymer. IR spectroscopy showed that there is no interaction of drug with polymer. In the present study, direct compression was used to prepare the tablets. The powder mixtures were compressed into tablet using flat face multi punch tablet machine. Camphor was sublimed from the tablet by exposing the tablet to vacuum drier at 60°C for 12 hours. All the formulations were evaluated for their characteristics such as average weight, hardness, wetting time, friability, content uniformity, dispersion time (DT), and dissolution rate. An optimized tablet formulation (F 9) was found to have good hardness of 3.30 ± 0.10 kg/cm^2, wetting time of 42.33 ± 4.04 seconds, DT of 34.67 ± 1.53 seconds, and cumulative drug release of not less than 99% in 16 minutes.

Key words: Cinnarizine, contour plot, factorial design, orally disintegrating tablet, wetting time, water absorption ratio

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as "melt in mouth" or "mouth dissolve (MD)" tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime, lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability, make these tablets popular as a dosage form of choice in the current market.[1,2]

A broad range of drugs (cardiovascular, analgesics, narcoleptics, antihistamines, and antibiotics) can be considered candidates for this dosage form. Fast dissolving tablets are formulated by techniques like tablet molding,[3] spray drying,[4] lyophilization,[5] sublimation,[6] and addition of disintegrants.[7] Some of the patented technologies for preparation of fast dissolving tablets are Zydis,[8,9] OraSolv,[10] DuraSolv, Flash Dose,[11] Wow tab (Without Water), and Flashtab.[12]

Objective of this study was to formulate directly compressible orally disintegrating tablets of cinnarizine with sufficient mechanical integrity, content uniformity, and acceptable

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palatability to assist patients of any age group for easy administration for the treatment of vertigo/Meniere's disease, nausea and vomiting, and motion sickness for rapid dissolution and absorption of drug which may produce rapid onset of action. It is also helpful for vestibular symptoms of other origins. Cinnarizine inhibits contractions of vascular smooth muscle cells by blocking calcium channels. It increases erythrocyte deformability and reduces blood viscosity. It inhibits stimulation of the vestibular system.[13] Cinnarizine is rapidly absorbed after oral dose. Peak plasma concentration occurs 2 to 4 hours and its plasma half-life is about is about 3 to 4 hours after an oral dose. It is water insoluble and tasteless. Therefore, it was selected as a model drug for the preparation of mouth dissolving tablets.[14]

MATERIALS AND METHODS

Materials

Cinnarizine and crosscarmellose sodium (CCS) was purchased from Yarrow Chemicals and Pharmaceutical (Mumbai, India). Sodium starch glycolate (SSG) and microcrystalline cellulose was obtained as a gift sample from Maple biotech India Pvt. Ltd (Pune, India). Camphor was obtained from Research Lab., Sodium saccharine and Magnesium Stearate was purchased from Fine chemicals. All other ingredients were of analytical grade.

Methods

Calibration curve of cinnarizine

Solutions of cinnarizine (2, 4, 6, 8, 10, 12 µg/ml) was prepared using phosphate buffer pH 1.2 and absorbance was measured using UV-Visible spectrophotometer (Shimadzu 1700, Japan) at 254 nm [Figure 1].

Preparation of cinnarizine fast dissolving tablets

All the raw materials were passed through 80 mesh screen prior to mixing. Cinnarizine, all excipients, and a subliming material, i.e., camphor, were physically mixed using mortar for 15 minutes. An optimized concentration of camphor was added to aid the porosity of the tablet. The addition of sweetener impacts satisfying taste to the formulation. A 3^2 full factorial design was applied to study the combined effect of two formulation variables: Amount of SSG and CCS. Then, the powder mixture was lubricated with 1% magnesium stearate and compressed into tablets using flat face 9-mm diameter rotary tablet punching machine (Hardik Eng. Pvt. Ltd, Ahmedabad). The resulting tablets were kept for sublimation for 12 hours in vacuum drier (Usico Vaccum Oven, Model No.79, 380 mm Hg) at 60°C. The composition of preliminary batch to optimize the amount of camphor and the factorial batch has been shown in Tables 1 and 2 respectively. After optimizing the amount of camphor, 50 tablets of each batch (9 batches) were prepared for the further evaluation as per 3^2 full factorial designs.

3^2 Full Factorial Designs

A 3^2 full factorial design was applied to examine the combined effect of two formulation variables, each at 3 levels, and the possible nine combinations of cinnarizine tablets were prepared [Table 2]. The amount of SSG (X_1) and the amount of CCS (X_2) were taken as independent variables. The dispersion time (DT) and % friability were taken as dependent variables[15] [Tables 3 and 4].

EVALUATION OF PREPARED CINNARIZINE FAST DISSOLVING TABLETS

Weight Variation

Twenty tablets were randomly selected from each formulation and weighed using a Shimadzu digital balance (Type-AUY 220. No.-D449811085). The mean SD values were calculated.[16]

Thickness

Ten tablets from each formulation were taken randomly and their thickness was measured with a digital screw gauge

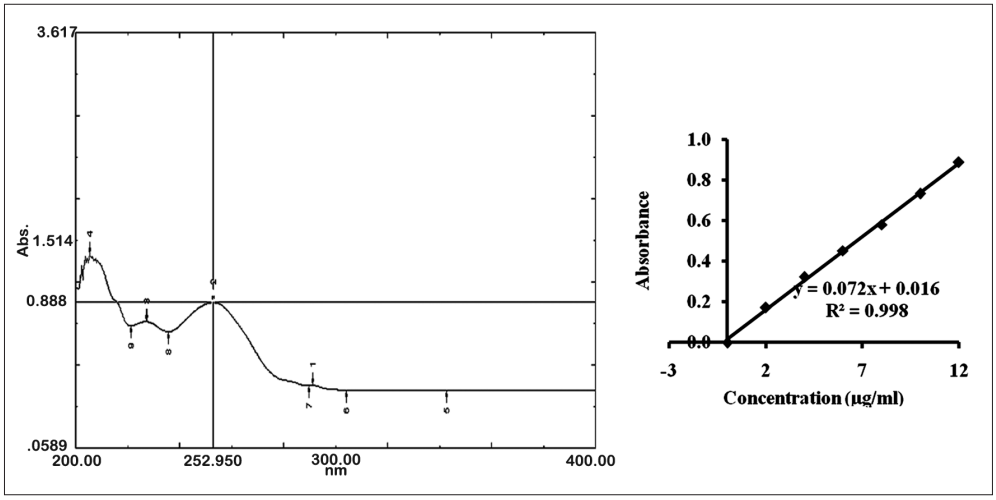

Figure 1: Standard curve of cinnarizine using 1.2 pH phosphate buffer at 254 nm

Table 1: Composition of preliminary batch to optimize the amount of camphor

Ingredients (mg)	Formulation code			
	PB1	PB2	PB3	PB4
Cinnarizine	25	25	25	25
Camphor	5	10	15	20
Sodium starch glycolate	8	8	8	8
Crosscarmellose sodium	8	8	8	8
Microcrystalline cellulose*	qs	qs	qs	qs
Sodium saccharine	3	3	3	3
Magnesium stearate	3	3	3	3
Dispersion time (sec)	85	47	39	31
% Friability	0.33	0.46	1.1	1.5

*Microcrystalline cellulose (qs) means "quantity sufficient" to make the total weight of 1 tablet of 100 mg

Table 2: Composition of various batches of cinnarizine tablets as per 3^2 full factorial design

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Cinnarizine	25	25	25	25	25	25	25	25	25
Sodium starch glycolate	8	8	8	10	10	10	12	12	12
Crosscarmellose sodium	8	10	12	8	10	12	8	10	12
Camphor	10	10	10	10	10	10	10	10	10
Microcrystalline cellulose	qs	qs	qs	qs	qs	qs	qs	qs	qs
Sodium saccharine	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3

qs: Quantity sufficient

Table 3: Formulation and dispersion time, and friability characteristics of batches in 3^2 factorial designs*

Formulation code	Coded value		Dispersion time DT ± SD (sec)	Friability (%F) ± SD
	X_1	X_2		
F1	-1	-1	56.67 ± 3.05	0.6026 ± 0.10
F2	-1	0	47.33 ± 2.52	0.5081 ± 0.10
F3	-1	1	54.00 ± 3.60	0.4893 ± 0.07
F4	0	-1	56.00 ± 3.60	0.7291 ± 0.14
F5	0	0	61.67 ± 2.08	0.5183 ± 0.20
F6	0	1	60.33 ± 1.53	0.5902 ± 0.08
F7	1	-1	37.33 ± 2.08	0.7609 ± 0.11
F8	1	0	39.33 ± 2.52	0.6250 ± 0.28
F9	1	1	34.67 ± 1.53	0.6227 ± 0.23
Check point	-0.2	+0.8	36.77 ± 1.57	0.4991 ± 0.08

*X_1 indicates amount of sodium starch glycolate (mg); X_2, amount of crosscarmellose sodium (mg); DT: Dispersion time; and F: Friability

Table 4: Amount of variables in a 3^2 factorial design*

Coded values	Actual values	
	X_1:SSG	X_2:CCS
-1	8	8
0	10	10
1	12	12

X_1 indicates amount of sodium starch glycolate (mg); X_2, amount of crosscarmellose sodium (mg); DT: Dispersion time; and F: friability. Camphor was sublimed by heating tablets in a vacuum oven

micrometer (Mitutoyo, Japan). The mean SD values were calculated.[16]

Hardness and Friability

Hardness or crushing strength of the tested orally disintegrating tablet formulations was measured using the tablet hardness tester (Monsanto type). The friability of a sample of 20 orally disintegrating tablets was measured utilizing a USP-type Roche friabilator (Camp-bell Electronics, Mumbai). Preweighed tablets were placed in a plastic chambered friabilator attached to a motor evolving at a speed of 25 rpm for 4 minutes (Lachman, 1991).[17] The tablets were then dedusted, reweighed, and percentage weight loss (friability) was calculated.

$$\%\,\text{Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Wetting Time

Five circular tissue papers were placed in a Petri dish of 10-cm diameter. Ten milliliters of water containing 0.5% eosin, a water-soluble dye, was added to the Petri dish. The dye solution was used to identify complete wetting of the tablet surface. A tablet was carefully placed on the surface of the tissue paper in the Petri dish at 25°C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. These measurements were carried out in replicate of six. Wetting time was recorded using a stopwatch.[18]

In vitro Dispersion Time

DT of the orally disintegrating tablets was determined following the procedure described by Gohel *et al*. (2004).[19] 10 ml of pH 6.8 phosphate buffer at 25°C was placed in a Petri dish of 10-cm diameter. The tablet was then carefully placed in the center of the Petri dish and the time required for the tablet to completely disintegrate into fine particles was noted. Measurements were carried out in replicates of six tablet ($n = 6$) and mean SD values were recorded.

In vitro Release Studies

In vitro release studies of cinnarizine from all formulations were performed according to USP XVIII apparatus II, paddle method (Dissolution testapparatus-TDT-06T, Electro lab, Mumbai, India). Paddle speed was maintained at 50 rpm and 900 ml of pH 6.8 phosphate buffers was used as the dissolution medium. Samples (10 ml) were collected at predetermined time intervals (every 2 minutes) and replaced with equal volume of fresh medium, filtered through a Whatman filter paper, and analyzed with a UV—Visible spectrophotometer at λ = 254 nm. Drug concentration was calculated from a standard calibration plot and expressed as cumulative % drug dissolved. The release studies were performed in replicates of three.[20]

Assay

All the formulations were assayed for drug content. Ten tablets were randomly selected from each formulation and pulverized to a fine powder. Weighed aliquots containing an amount of powder equivalent to a single dose were taken in triplicate and assayed for the drug content utilizing a UV-VIS spectrophotometer at a wavelength of 254 nm (Bi Y *et al*., 1996).[21]

3^2 Factorial Design

The amount of superdisintegrants SSG (X_1) and crosscarmelose sodium (X_2) were chosen as independent variables in a 3^2 full factorial design. A statistical model incorporating interactive and polynomial terms was used to evaluate the responses.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_1^2X_1^2 + b_2^2X_2^2 \quad (1)$$

Where, Y is the dependent variable, b_0 is the arithmetic mean response of the 9 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 1 factor at a time from its low to high value. The interaction terms (X_1X_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 nonlinearity. The DT and percentage friability for the 9 batches (F1 to F9) showed a wide variation (i.e., 34-61 seconds and 0.48%-0.76%, respectively). The data clearly indicate that the DT and percentage friability values are strongly dependent on the selected independent variables.

Data were further analyzed by Microsoft Office-2007 for regression analysis. Analysis of variance (ANOVA) was implemented to assure no significant difference between developed full model and reduced model. Contour plots were plotted to study response variations against two independent variables using Design Expert 8 software.

RESULTS AND DISCUSSION

A total of nine formulations were prepared and evaluated. The preliminary trials were conducted to optimize the concentration of subliming material camphor for which four preliminary batches were prepared using 0 to 20 mg concentration of camphor, results of which showed that as the concentration of camphor increases, the porosity of tablet goes on increasing, which showed fastest disintegration, but due to higher porosity, the tablet becomes more fragile. The promising result was shown by batch PB2 containing 10 mg of camphor (DT-47 seconds, Friability-0.46%). Hence, for further studies, 10 mg of camphor was optimized [Table 1].

In all the formulations, weight variations were within ±2.47% and hardness was within ±0.15%. All the formulations pass the drug content assay. Uniformity of drug contents was more than 95% in all the formulations. Friability data of preliminary batches represent that as the concentration of camphor increases, % friability of the formulation also increases. All the formulation passed %friability limit.

Wetting time was determined for all the formulations. Wetting time of all the formulation were more than 42 seconds, due to its rapid water-absorbing nature, involving both capillary and swelling mechanisms of SSG and CCS. DT is an important criterion for selecting an optimum orally disintegrating tablet formulation. It was observed that when the superdisintegrants concentrations are increased, DT were also decreased. F7, F8, and F9 batches have the lower DT as compared with other formulation and these batches did not cross the friability limit; so, while considering friability and DT F9 batch having maximum superdisintegrant concentration was optimized batch with 34.67 seconds DT and 0.62% friability.

Infrared Studies

The Infrared (IR) spectra were determined following the procedure described by Bhupendra GP *et al*. (2010). The IR spectra of optimized batch and cinnarizine were studied and confirmed that there is no interaction with each other. The spectra show all the prominent peaks of drug [Figure 2]. The results of all formulations have been shown in Table 5. The batch F9 was found to be optimized formulation. The F9 batch has least DT and least wetting time. The hardness of tablets was found to be 3.30 ± 0.10 kg/cm^2. The wetting time and disintegration time were found to be 42.33 ± 4.04 seconds and 34.67 ± 1.53 seconds, respectively. The optimized batch shows more than 99% release in 16 minutes [Figure 3].

In Vitro Drug Release Studies

Dissolution methods for orally disintegrating tablets are similar to approaches taken for conventional tablets. All of the orally disintegrating tablet formulations released more than 80.0% of the drug within 10 minutes [Figure 3]. *In vitro* DT considering wetting time, *in vitro* DT, %friability, and cumulative % drug released, formulation F9 was considered to be better than less amount of CCS and SSG. F9 was considered as the optimal orally disintegrating tablet formulation among all of the nine formulations tested in this study.

Factorial Design

The amounts of the superdisintegrants (SSG, X_1 and CCS, X_2) were chosen as independent variables in a 3^2 full factorial design. A statistical model incorporating interactive and polynomial terms was used to evaluate the responses (equation 1).

The disintegration time and percentage friability for

the nine batches (F1 to F9) showed a wide variation (i.e., 34-61 seconds and 0.489% - 0.760%, respectively). The data clearly show that the disintegration time and percentage friability values are strongly dependent on the selected independent variables. The fitted equations (full and reduced) relating the responses disintegration time and percentage friability to the transformed factor are shown in Table 6. The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (i.e., positive or negative). Table 7 shows the results of the analysis of variance (ANOVA), which was performed to identify insignificant factors. The high values of correlation coefficient for disintegration time and percentage friability [Table 7] indicate a good fit. The equations may be used to get estimates of the response as a small error of variance was noticed in the replicates. The significance test for regression coefficients was performed by applying the Student *t test*. A coefficient is significant if the calculated *t* value is greater than the critical value of *t*.

Full and Reduced Model for Dispersion Time

The significance level of coefficient b_2, b_{22}, and b_{12} was found to be *P*=0.9088, 0.7503, and 0.9989, respectively;

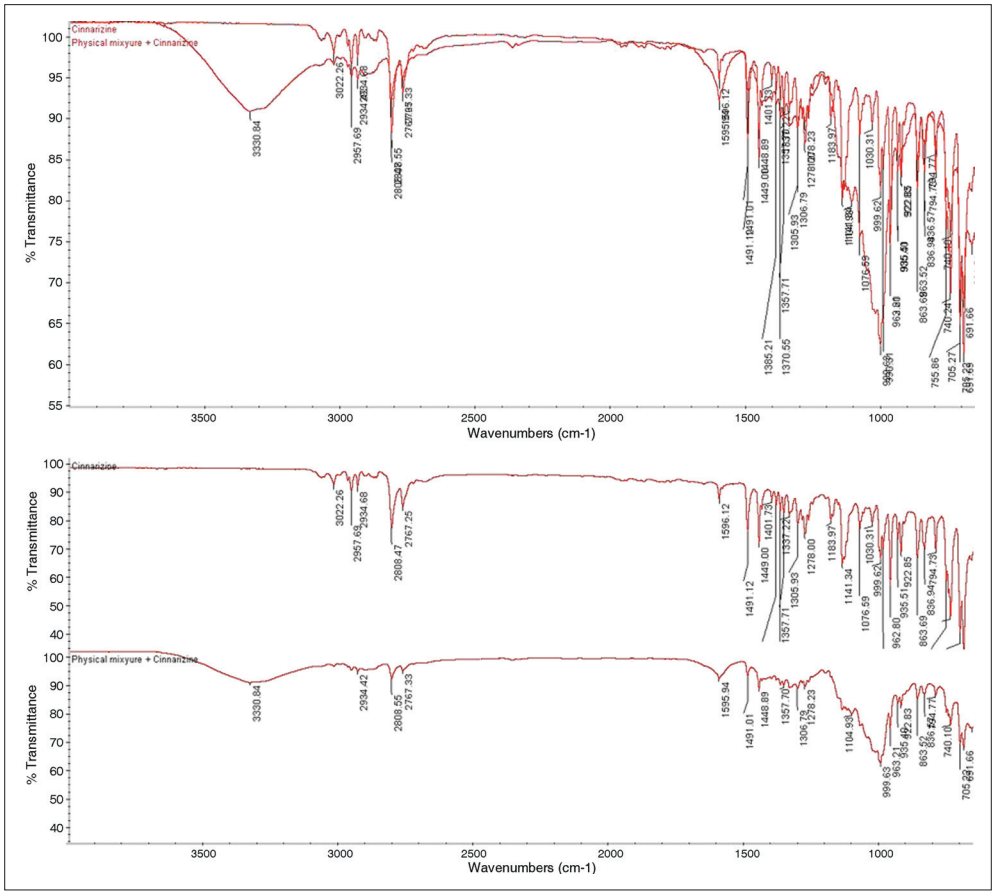

Figure 2: IR spectra of pure drug and optimized batch (F9)

Table 5: Evaluations of all batches of cinnarizine tablets

Formulation code	Average weight (mg) ± SD (*n*=3)	Hardness (kg/cm²) ± SD (*n*=3)	Wetting time (sec.) ± SD (*n*=6)	Friability (%) (*n*=3)	Content uniformity	Dispersion time (sec) ± SD (*n*=6)
F1	98.16 ± 1.83	3.37 ± 0.06	65.00 ± 2.00	0.6026 ± 0.10	97.26	56.67 ± 3.05
F2	98.70 ± 2.47	3.37 ± 0.15	58.33 ± 4.04	0.5081 ± 0.10	100.58	47.33 ± 2.52
F3	98.98 ± 2.25	3.03 ± 0.06	67.33 ± 5.03	0.4893 ± 0.07	97.95	54.00 ± 3.60
F4	99.05 ± 2.25	3.03 ± 0.06	68.00 ± 3.00	0.7291 ± 0.14	96.57	56.00 ± 3.60
F5	99.18 ± 2.10	3.47 ± 0.06	61.00 ± 4.00	0.5183 ± 0.20	97.67	61.67 ± 2.08
F6	98.48 ± 1.92	3.90 ± 0.10	64.67 ± 9.29	0.5902 ± 0.08	95.87	60.33 ± 1.53
F7	99.26 ± 2.03	3.10 ± 0.10	44.33 ± 5.03	0.7609 ± 0.11	97.40	37.33 ± 2.08
F8	99.66 ± 2.38	3.03 ± 0.06	43.00 ± 7.21	0.6250 ± 0.28	98.09	39.33 ± 2.52
F9	98.51 ± 2.18	3.30 ± 0.10	42.33 ± 4.04	0.6227 ± 0.23	99.47	34.67 ± 1.53

hence, it was omitted from the full model to generate the reduced model. The results of statistical analysis are shown in Table 6. The coefficients b_1, b_2, and b_{22} were found to be significant at $P<0.05$; hence, they were retained in the reduced model. The reduced model was tested in portions to determine whether the coefficient b_{11} and b_{12} contributes significant information for the prediction of disintegration time or not. The results for testing the model in portions are shown in Table 7. The critical value of F for $\alpha=0.05$ is equal to 4.46 (df=2, 8). Since the calculated value (F=0.0412) is less than the critical value (F=4.46), it may be concluded that the interaction term b_{11} and b_{12} does not contribute significantly to the prediction of disintegration time and therefore can be omitted from the full model. For drawing conclusions, grid search technique of contour plot should be used since one of the polynomial terms (b_{22}) is also significant. The results of multiple linear regression analysis (reduced model) reveal that on increasing the concentration of either SSG or CCS, a decrease in disintegration time is observed; both the coefficients b1 and b2 bear a negative sign. When higher percentage of camphor is used, higher porosity is expected in the tablets. The water uptake and subsequent disintegration are thus facilitated. It is obvious that in the presence of higher percentage of superdisintegrants, wicking is facilitated.

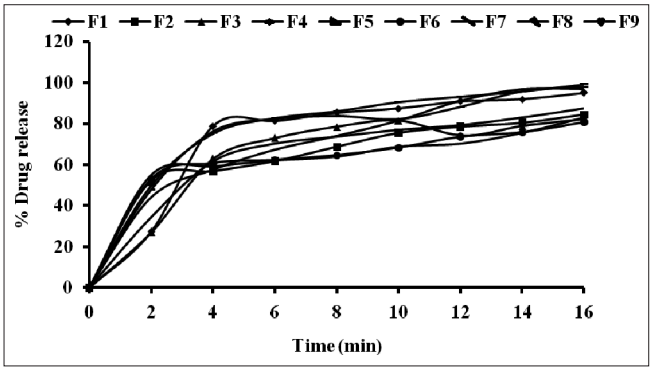

Figure 3: Dissolution profile of all batches in 6.8 pH buffer

Full and Reduced Model for Percentage Friability

The significance level of coefficients b_{11}, and b_{12} were found to be greater than P=0.05; hence, they were omitted from the full model to generate the reduced model. The

Table 6: Summary of results of regression analysis*

Response (% friability)	b_0	b_1	b_2	b_{11}	b_{22}	b_{12}
For percentage friability						
FM	0.53	0.068	−0.065	5.272E-003	0.098	−6.225E-003
P values	0.0005	0.0007	0.0009	0.7697	0.0008	0.6785
RM	0.53	0.068	−0.065	-	0.10	-
P values	0.0001	0.0001	0.0002	-	0.0001	-
Response (dispersion time)						
For dispersion time						
FM	60.86	−7.78	−0.17	−15.52	−0.68	2.500E-003
P values	0.0005	0.0009	0.9088	0.0001	0.7503	0.9989
RM	60.67	−7.78	-	−15.78	-	-
P values	0.0001	0.0001	-	0.0001	-	-

*FM indicates full model; and RM: Reduced model

Table 7: Calculations for testing the model in portions*

For percentage friability	DF	SS	MS	F	R^2	
Regression						*Fcalc* =
FM	5	0.086	0.017	20.75	0.9368	*Ftable* = 4.74
RM	3	0.086	0.029	42.64	0.9343	DF = (2,7)
Error						
FM	7	5.803E-003	8.290E-004	-	-	
RM	9	6.035E-003	6.705E-004	-	-	
For dispersion time						
Regression						*Fcalc* = 0.041208
FM	4	1168.82	292.21	28.22	0.9339	*Ftable* = 4.46
RM	2	1167.53	583.76	69.38	0.9328	DF = (2,8)
Error						
FM	8	82.68	11.81	-	-	
RM	10	84.14	8.41	-	-	

*DF indicates: Degrees of freedom; SS: Sum of squares; MS: Mean of squares; F: Fischer's ratio; R^2: Regression coefficient; FM: Full model; and RM: Reduced model

results of statistical analysis are shown in Table 6. The coefficients b1 and b2 were found to be significant at $P<0.05$; hence, they were retained in the reduced model. The reduced model was tested in portions to determine whether the coefficients b_{11} and b_{12} contribute significant information for the prediction of disintegration time or not. The results for testing the model in portions are depicted in Table 7. The critical value of F for $\alpha=0.05$ is equal to 4.74 (dF=2,7). Since the calculated value (F=0.1369) is less than the critical value (F=4.74), it may be concluded that the interaction term and polynomial terms do not contribute significantly to the prediction of disintegration time. Hence, conclusions can be drawn considering the magnitude of the coefficient and the mathematical sign (positive or negative) it carries. An increase in the concentration of camphor leads to an increase in friability, because the coefficient b1 bears a positive sign. When a higher percentage of camphor is used, more porous tablets are produced, which are mechanically weak. The increase in the concentration of CCS results in decreased friability values. CCS is known to produce mechanically strong tablets. Analysis of contour plot, shown in Figures 4 and 5 reveals that the whole of the contour area has acceptable friability values (0.1%-0.35%). It was arbitrarily decided to select a batch of tablets that disintegrate in less than 40 seconds. The final selection is done after considering other aspects such as ease of manufacturing, cost, etc. In industry, the total time required for manufacturing a dosage form is of prime concern. A checkpoint batch F10 was prepared at $X_1 = -0.2$ level and $X_2 = 0.8$. From the reduced model, it is expected that the friability value of the checkpoint batch should be 0.45 and 0.57, and the value of disintegration time should be 38.6 seconds. Table 2 indicates that the results are as expected. Thus, we can conclude that the statistical model is mathematically valid. The factorial design batches were subjected to short-term stability studies at 40°C and 75% RH for 6 months. Studies indicated that no significant change in appearance of the tablets, disintegration time, and percentage friability were observed.

Contour Plot

It was observed that DT and % friability were dependent on both the factors. There was a linear decrease in the DT with increase in the levels of both factors [Figures 4 and 5]. The model F-value of 20.75 implies the model is significant for % friability and the model F-value of 28.22 implies the model is significant for DT. "Adeq Precision"

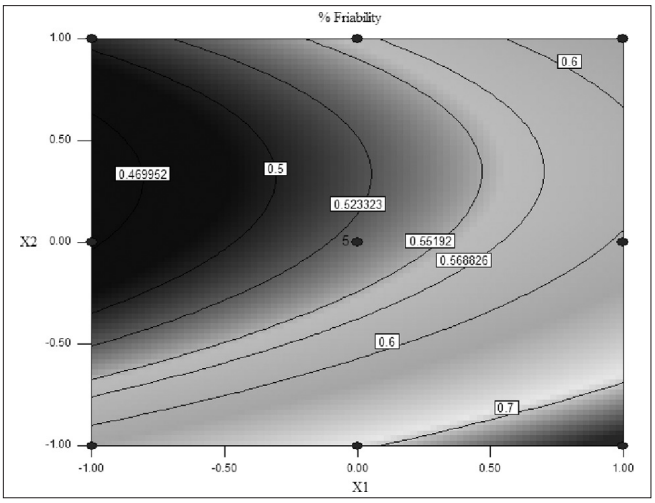

Figure 4: Contour plot for % friability

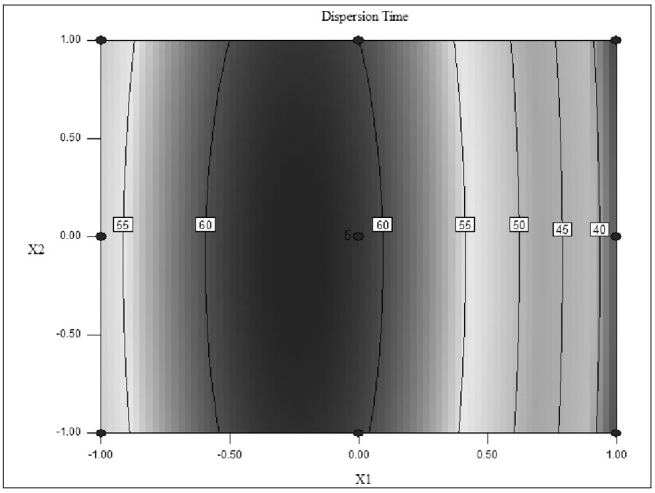

Figure 5: Contour plot for dispersion time

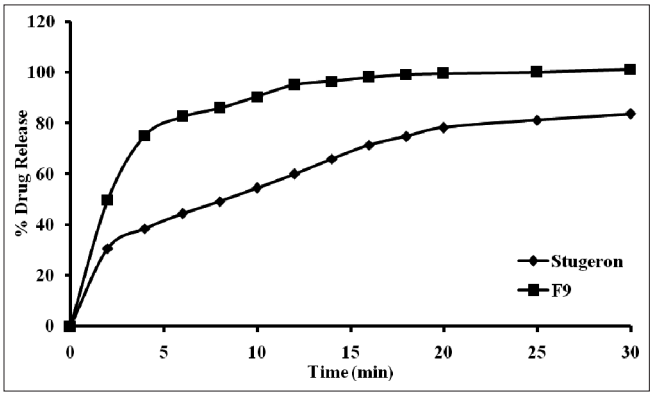

Figure 6: Comparative profile of dissolution study of mouth dissolving tablet of cinnarizine with marketed formulation (conventional)

Table 8: Comparison between one marketed product and selected formulation (F9)

Formulation code	Average weight (mg) ± SD (n=3)	Hardness (Kg/cm^2) ± SD (n=3)	Wetting time (sec.) ± SD (n=6)	Friability (%) (n=3)	Content uniformity	Disintgration time (sec) ± SD (n=6)
Marketed product	197 ± 1.55	4.13 ± 0.31	175.67 ± 22.50	0.7734 ± 0.17	96.77	304.33 ± 14.29
F9	98.51 ± 2.18	3.30 ± 0.10	42.33 ± 4.04	0.6227 ± 0.23	99.47	34.67 ± 1.53

measures the signal to noise ratio. A ratio greater than 4 is desirable. The ratio of 10.342 indicates an adequate signal for DT and the ratio of 15.637 indicates an adequate signal for % friability. This model can be used to navigate the design space.

Comparison between conventional marketed product and selected formulation

A marketed conventional cinnarizine tablet was compared with the selected formulation F9 and results are reported in Table 8. Mouth dissolving tablets of cinnarizine is not available in the market. So, the selected formulation F9 was compared with conventional dosage form (Stugeron, Johnson and Johnson). Comparative profiles of dissolution study are shown in Figure 6. Cumulative percent drug release from the marketed formulation was 71%, whereas 99% from the F9 in 16 minutes. From the comparison, it was concluded that F9 formulation is more effective than the conventional dosage form of cinnarizine.

CONCLUSION

The goal of this investigation has been achieved by preparing fast drug delivery technique of cinnarizine with the aid of super disintegrating agents and a subliming material. The results of a 3^2 full factorial design revealed that the amount of camphor and superdisintegrants significantly affect the dependent variables, disintegration time, and percentage friability. The optimized batch can be commercialized. Vacuum-drying technique would be a successful alternative approach compared with the utilization of more expensive adjuvants in the formulation of mouth dissolving tablets. Fast drug delivery techniques of cinnarizine administration without water, accuracy of dosage, easy portability, alternative to liquid dosage forms, ultimate for pediatric and geriatric patients, and quick onset of action. It is thus concluded that by adopting a logical formulation approach, an optimum point can be reached in the shortest time with minimum efforts.

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