WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 7, 1781-1799. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF CINNARIZINE

Anchal Sharma* and Rajeev Garg

ASBASJSM College of Pharmacy, Bela, Ropar.

Article Received on
16 May 2016,
Revised on 06 June 2016,
Accepted on 27 June 2016
DOI: 10.20959/wjpr20167-6635

***Corresponding Author**
Anchal Sharma
ASBASJSM College of Pharmacy, Bela, Ropar.

ABSTRACT

Cinnarizine is an H1 antihistaminic drug used in the treatment of motion sickness, vomiting and vertigo. Vertigo and vomiting is a significant public health concern in many developed and developing countries. Thus formulating Cinnarizine mouth dissolving tablet would provide fast relief. But it is insoluble in water. So in this work an attempt was made to increase the solubility by using solid dispersion technique by using PVP K30 as a carrier and to formulate the mouth dissolving tablet. The solid dispersion was characterized for solubility, IR and XRD studies. Using solid dispersion and by adding superdisintegrants i.e SSG and crospovidone in different concentration mouth dissolving tablet was formulated. The tablet was evaluated for thickness, hardness, weight variation, friability, drug content, disintegration time and dissolution studies. The disintegration time was found between 22-52 second and the percent drug release was found 69.21-98.80. The results showed that solubility of Cinnarizne was successfully enhanced and formulated into an mouth dissolving tablet as an alternative to conventional tablets.

KEYWORDS: Cinnarizne, Solid dispersion, PVP K30, crospovidone, SSG, Mouth dissolving tablet, IR,XRD.

INTRODUCTION

Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency, and the production of more cost-effective dosage forms[1].

Even though the oral drug route is preferred it can be problematic for number of reasons the most significant contributors being poor aqueous solubility or poor membrane permeability of the drug molecule. The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro-intestinal fluids often cause insufficient bioavailability and presents one of the major challenges to formulation scientists in the industries here are many approaches for enhancing solubility like solubilization, complexation, particle size reduction, salt formation etc., but each of them has practical limitations. 1n 1961, Sekiguchi and Obi developed a practical method whereby many of the limitations with the bioavailability enhancement of poorly water soluble drugs can be overcome.[2] The method was termed as "solid dispersion". Solid dispersion is a promising drug delivery forms, which offer the possibility to disperse a hydrophobic drug in a hydrophilic matrix and thereby improve the dissolution rate and bioavailability of the drug. Cinnarizine is an H1 antihistaminic drug used in the treatment of motion sickness, vomiting and vertigo.

Cinnarizine has poor aqueous solubility. In the present study an attempt was made to increase the solubility of drug Cinnarizine and thus to formulate mouth dissolving tablet.

EXPERIMENTAL

MATERIAL AND METHOD

Cinnarizine was received as gift sample from Dr. Kumar Pharmaceuticals. PVP K30, aspartame and magnesium stearate were procured from Loba Chem Pvt. Ltd. Sodium starch glycolate and Crospovidone were procured from Signet Chemicals. Mannitol, Citric acid and Sodium Bicarbonate were procured from HIMEDIA. Methanol was purchased from SD Fine chemicals. All the chemicals used were of analytical grade.

PREFORMULATION STUDY

Melting Point

The melting point of the drug (Cinnarizine) was determined by capillary fusion method. A capillary sealed at one end was filled with small amount of drug and the capillary was kept inverted i.e. sealed end downwards into the melting point apparatus. The temperature at which the solid drug converts into liquid was noted down with the thermometer.

Solubility Study: Solubility of drug was determined by taking excess amount of drug in 10ml of distilled water, 10mg of drug in 10ml phosphate buffer pH 6.8, 10mg of drug in 10ml

of 0.1N HCl. All these were kept on mechanical shaker for 24 hours and further dilutions were made i.e 20µg/ml respectively and absorbance was determined at 253nm.

Fourier transform infrared spectral assignment: The FTIR analysis of sample was carried out for qualitative compound identification. The infrared spectrum of Cinnarizine was performed on Fourier transformed infrared spectrophotometer. The sample pellet was mounted in IR compartment and scanned at wavelength 4000 – 400 cm.

X-Ray Powder Differactometry

Powder X-ray diffraction (XRD) pattern of pure drug and solid dispersions were recorded using X-ray diffractrometer. Under the following conditions: Target CuKa monochromatized radiation, voltage 40 KV and current 40 mA at ambient temperature. The data were collected in the conditions scan mode using a step size of 0.01^{O} at 20/sec. The scanned range was 5-70^{O}.

PREPARATION OF SOLID DISPERSION OF DRUG CINNARIZINE

Kneading method was used for preparation of solid dispersion. Because the solubility was found less so it was necessary to increase the solubility. Solid dispersion technique was used for solubility enhancement because of dispersion ability of drug. PVP K30 was used as carrier for the preparation of solid dispersion. For the solubility enhancement drug and carrier was mixed in 1:1, 1:2 and 1:3 ratio. For the preparation of solid dispersion 10mg of drug was taken and was mixed with 10mg, 20mg and 30mg PVP K30 polymer respectively. Methanol was used as co-solvent to form solid dispersion. These solid dispersion was dried for 48 hours and then passed through 60 mesh sieve and was stored for further use.

CHARECTERIZATION OF SOLID DISPERSION

The prepared solid dispersion was characterised for solubility study. Further the best formulation was evaluated for Fourier Transform Infra-red (FTIR) spectroscopy and X-Ray diffraction studies.

Characterization of solubility

Solid dispersions equivalent to 10 mg of Cinnarizine were added to 10 ml of phosphate buffer pH 6.8 in 10 ml volumetric flasks. The volumetric flasks was capped properly and shaken at temp. 25°C in a temperature controlled water bath (Shaking water bath) for 24 h. Resultant samples containing undissolved solid dispersions suspended in the volumetric flasks was

filtered through Whatman filter paper no. 41, suitably diluted with phosphate buffer pH 6.8 upto 20µg/ml and analyzed by UV spectrophotometer at 253.0 nm.

Fourier transforms infrared (FTIR) spectroscopy Fourier transform infrared (FTIR) spectrum of pure drug, and solid dispersion were recorded on samples prepared in potassium bromide (KBr) disks. Samples were prepared in KBr disks by means of a hydrostatic press. The scanning range was 4000 -400 cm^{-1}.

Powder X-ray diffraction (XRD) analysis

Powder X-ray diffraction (XRD) pattern of pure drug, and solid dispersions were recorded using X-ray diffractrometer. Under the following conditions: Target CuKa monochromatized radiation, voltage 40 KV and current 40 mA at ambient temperature. The data were collected in the conditions scan mode using a step size of 0.01°at 20/sec. The scanned range was 5-80°.

Preparation of Different Batches of Mouth Dissolving Tablets:

Different batches of mouth dissolving tablets were prepared by using superdisintegrants i.e crospovidone and soldium starch glycolate as in table 1.

Table 1: Preparation Of Different Batches Of Mouth Dissolving Tablet

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Solid Dispersion (mg) Drug=15mg	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
Crospovidone(mg)	2	4	6	-	-	-	2	4	6	2	4	6	2	4	6
SSG (mg)	-	-	-	2	4	6	2	2	2	4	4	4	6	6	6
Sodium Bicarbonate(mg)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Citric Acid (mg)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Aspartame (mg)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Mannitol (mg)	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Magnesium Stearate (mg)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Microcrystalline Cellulose (mg)	16	14	12	16	14	12	14	12	10	12	10	8	10	8	6

CHARACTERIZATION OF BLENDS

The quality of tablet, once formulated by rule, is generally dictated of physicochemical properties of blends. There are many formulations and process variables involved in mixing step and all these can affect the characteristics of the blend produced. The characterization of mixed blend was performed to find out the flow property of powder.

Bulk Density

Bulk density was determined by pouring a weighed quantity of tablet blend into graduated cylinder and measuring the height. Bulk density is the ratio of mass of tablet blend to bulk volume. It is expressed in g/cm^3. The bulk density was calculated by using the formula.[3]

Bulk density (ρb) = m/vb

=m/πr^{2}h

Where; m = weight of powder or granules (gm),

Vb = Bulk Volume (cm^3),

π = 22/7 = 3.14, r = Radius of Cylinder (cm),

h = Height reached by powder in cylinder (cm).

Tapped Density: Tapped density is ratio of mass of tablet blend to tapped volume of tablet blend. Accurately weighed amount of tablet blend poured in graduated cylinder and height was measured. Then cylinder was allowed to 100 tap under its own weight onto a hard surface. The tapping was continued until no further change in height was noted. [4]

Tapped density (ρt) = m/vt =m/πr^{2}h

Where; m = weight of powder or granules (gm),

v = Tapped Volume (cm^3),

π = 22/7 = 3.14,

r = Radius of Cylinder (cm),

h = Height reached by powder in cylinder after tapping (cm).

Carr's Index (Compressibility Index): Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder were determined, which is given as compressibility index. It is indirectly related to the relative flow rate. Compressibility index was determined by the given formula. [5]

Carr's Index = ρt – ρb/ρt × 100

Where; ρt = tapped density,

ρb= bulk density.

Hausner's Ratio

Hausner's ratio indicates the flow properties of powder & measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula:

Hausner's Ratio (Hr) = Tapped density/ bulk density

Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Angle of Repose (θ): Angle of repose was determined by using fixed funnel method. The fixed funnel method employ a funnel that was secured with its tip at a given height (2 cm), above the graph paper that was placed on a flat horizontal surface. Granules or tablet blend were carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. Thus, with r being the radius of the base of the conical pile. Angle of repose was calculated using the following equation:[6]

$\boldsymbol{\theta} = \mathbf{tan}^{-1}\ h/r$ Where; h = Height of pile, r = Radius of pile,

θ= Angle of repose.

EVALUATION PARAMETERS OF MOUTH DISSOLVING TABLETS

After compression of powder, the tablets were evaluated for organoleptic characteristics like colour, odour, thickness and physical characteristics like hardness, friability, disintegration time, wetting time and dissolution studies.[7-13]

General Appearance: The general appearance of a tablet, its visual identification and over all 'elegance' is essential for consumer acceptance. This includes tablets size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws, consistency and legibility of any identifying marking.

Uniformity of Weight: As per IP, twenty tablets were taken and weighed individually and collectively using digital balance. The average weight of one tablet was calculated. The weight variation test would be satisfactory method of determining the average weight of tablet.

Table 2: Weight Variation Limit for Tablet as per IP

Average Weight of Tablets(mg)	Maximum % Deviation Allowed
80 or Less	10
80-250	7.5
More then 250	5

Tablet Hardness: It can be defined as the force required per unit area to break the tablet. The hardness test was carried out using a tablet hardness tester (Hardness Tester, D.R. Schleunger, 6D tablet tester, Germany). Six tablets from each formulation batch were tested randomly, and the average reading was noted. The average hardness is measured in kg/cm.

Friability: Friability of the tablets was determined using Roche friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm for 4 min and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets i.e 6.5 gm was placed in the friabilator and were subjected to 100 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed. The friability (% f) was determined by the formula.

$$\% f = \mathbf{W0} - \mathbf{W1} / \mathbf{W0} \times 100$$

Where; % f = Percentage friability,

W0 = Initial weight (Before test),

W1 = Final weight (After test).

The accepted value should not more than 1% to pass in friability.

Disintegration Test

Disintegration of mouth dissolving tablets is achieved in the mouth owing to the action of saliva. To determine the disintegration time of tablet phosphate buffer equivalent to pH 6.8 was used. The temperature was kept 37±2°C. A cylindrical vessel was used in which 10-meshscreen was placed to determine disintegration time. 6 tablets were taken randomly and were placed in the vessels containing 10 mesh sieves. Disintegration time was determined for each tablet and average time was calculated.

Wetting Time: The method was followed to measure tablet wetting time. A piece of tissue paper (12 cm*10.75 cm) folded twice was placed in a small petridish (ID = 65 cm) containing 10 ml of phosphate buffer (pH 6.8), A tablet was put on the paper, and the time for the complete wetting was measured.

Drug Content Uniformity: For the content uniformity test, ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 100 mg of Cinnarizine was extracted into phosphate buffer solution pH 6.8 and liquid was filtered through Whatman filter paper. The Cinnarizine content was determined by measuring the absorbance at 253 nm after appropriate dilution with methanol. The drug content was determined using standard curve.

In-vitro Dissolution Studies: The in-vitro dissolution study was carried out in USP Dissolution Test Apparatus, (Type 2 paddle type). 900 ml of 0.1N HCl was used as dissolution medium. The temperature of dissolution media was maintained at 37±0.5ºC. The

paddle rotation speed was kept at 50 rpm. 5ml of the sample was withdrawn at various interval for 4 minutes for mouth dissolving tablets and the same volume was replaced with fresh dissolution media and was assayed spectrophotometrically at 253nm. Concentrations were calculated using calibration curves developed in respected media.

Optimization of Formulations

Selection of suitable experimental design

A 3^2 Full factorial design (FFD) was chosen for the current formulation optimization study. In a full factorial design, all the factors are studied in all the possible combinations, as it is considered to be most efficient in estimating the influence of individual variables (main effects) and their interactions, using minimum experimentation. Concentrations of two superdisintigrants (sodium starch glycolate and crospovidone) were selected as independent factors whereas disintegration time (DT), percentage friability (%F) and percentage drug release were measured as responses. Based on initial trials, levels of SSG and crospovidone were selected. Nine formulations were prepared for both superdisintegrants according to 3^2 factorial designs and evaluated. The responses were analyzed for ANOVA using Design Expert version 9. A mathematical equation was generated for each response parameter. The mathematical models were tested for significance. Response surface plots were generated for each response to study the behaviour of the system.

Generation of statistical model

A statistical model, $Y = b_0 + b_{1X1} + b_{2X2} + b_{12X1X2} + b_{11}(X_1)^2 + b_{22}(X_2)^2$, incorporating interactive and polynomial terms was used to evaluate the responses; where Y is the dependent variable, b_0 is the arithmetic mean response of the nine runs and bi is the estimated coefficient for the factor Xi. 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 term ($_{X1X2}$) indicates the interaction between two factors. The polynomial terms $(X_1)^2$ and $(X_2)^2$ are included to investigate nonlinearity.

RESULT AND DISCUSSION

PREFORMULATION STUDIES

Physical Appearance and Melting Point

The Sample of Cinnarizine was analysed for various organoleptic, physicochemical and spectrophotometric methods. The sample possesses similar colour, odour, taste and texture as given in officials (Indian pharmacopoeia).

Table 3: **Organoleptic Characters**

PROPERTIES	INFERENCE
Colour	White or almost white powder
State	Amorphous
Odour	Odourless

Table 4 Melting Point Determination

Drug	Melting Point	
Cinnarizine	**Litrature Value**	**Experimental Value**
	118-122ºC	119-123°C

SOLUBILITY STUDY

The solubility of pure drug and solid dispersion in phosphate buffer pH 6.8 at 20µg/ml is shown in table.

Table 5 Solubility Study

Formulation Number	Solubility(µg/ml)
Pure Drug	0.176
SD1	2.01
SD2	3.12
SD3	4.49

Because the solubility of SD3 was found maximum so it was selected for final formulation.

FTIR Study:

FTIR of pure drug and solid dispersion is shown in fig.

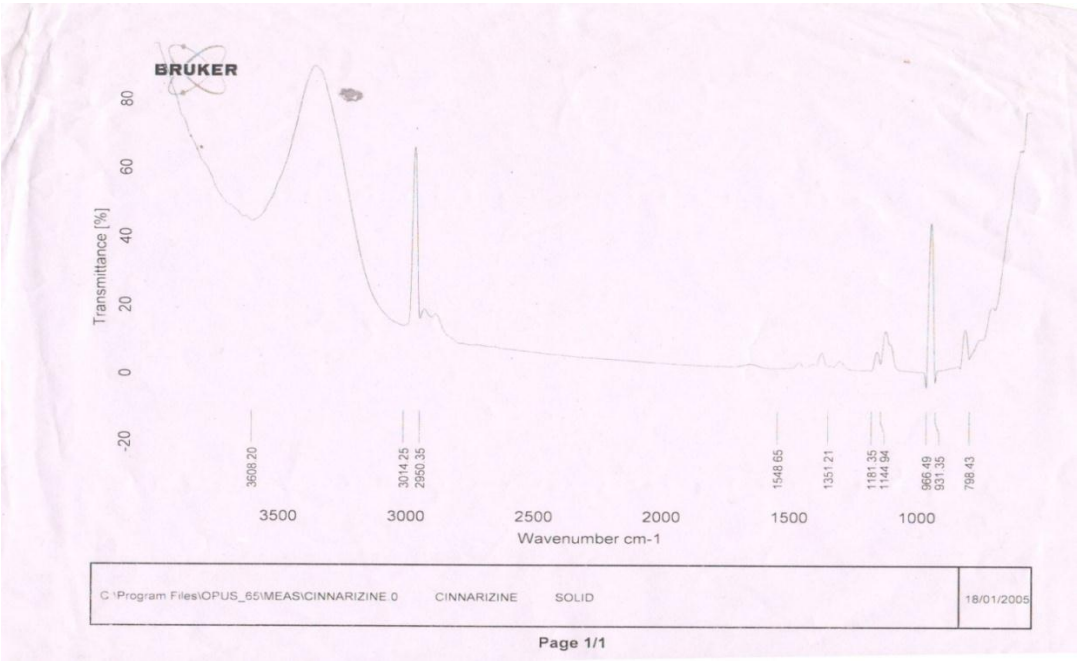


Fig: 1

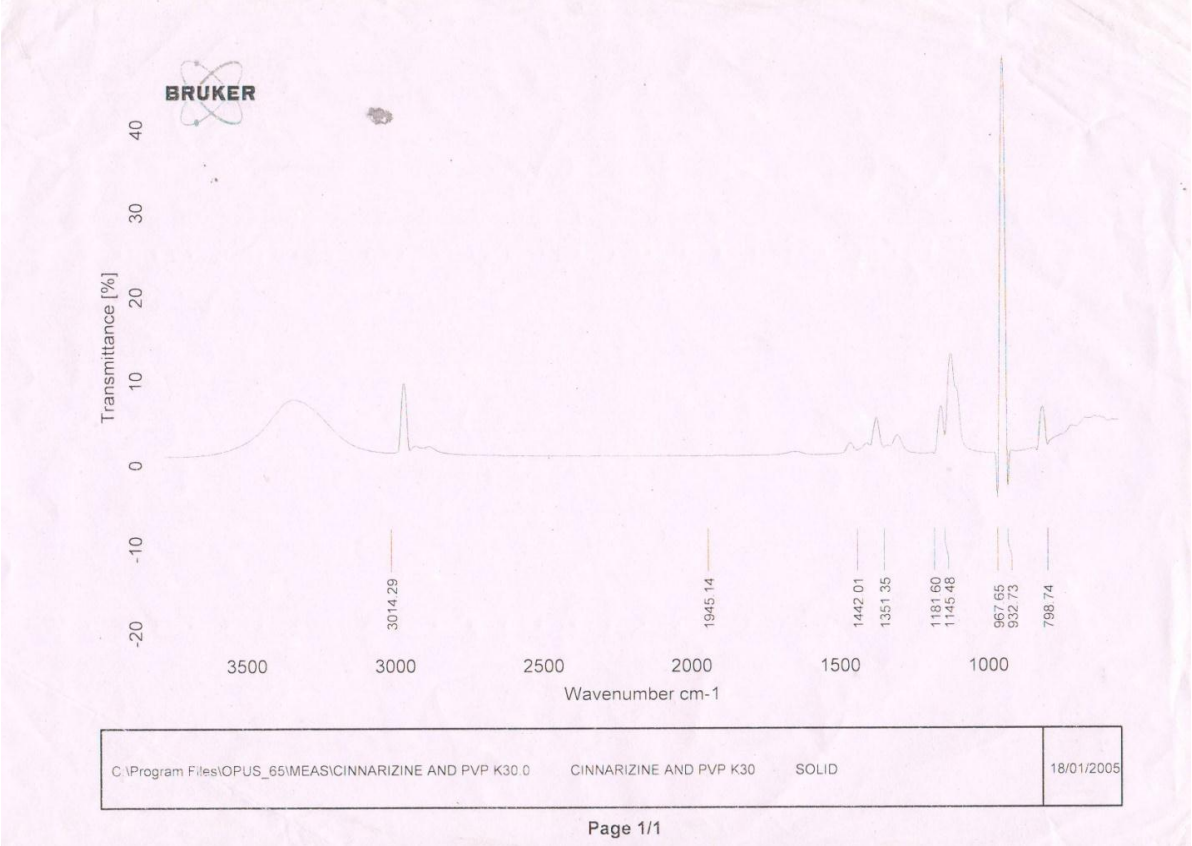


Fig: 2

FTIR spectrum of pure Cinnarizine revealed the presence of charecteristics peak at 3608.20 cm-1 (aromatic C-N stretch), 2950.35 cm-1 (aliphatic C-H stretch), 1548.65cm-1 (C=C aliphatic streaching), 1351.21 cm-1,1181.35cm-1,1144.94cm-1 (aliphatic C-H stretch), respectively. No major differences were observed in characteristics absorption peaks in comparison to spectrum of pure drug. There were no extra peaks observed in the FTIR spectrum of solid dispersion. This established that the drug Cinnarizine and PVP K30 used in the study showed no interaction and indicated that they were compatible with each other. This is shown in Fig 1 and 2.

XRD Study: The X-ray diffract gram of pure cinnarizine and formulation are shown in fig. XRD pattern of pure Cinnarizine and solid dispersions are shown in fig 5.6, 5.7 respectively. In the X-ray diffractrogram of Cinnarizine, sharp peaks at diffraction angle (2θ) were 10.12^{O}, 13.15^{O}, 17.60^{O}, 20.76^{O}, 24.62° indicate the presence of highly crystalline in nature while solid dispersions shows sharp peak at 18.62^{O} and 20.9^{O}. This revealed less number of peaks in the solid dispersions. This finding confirms the presence of little amount of crystalline drug in the solid dispersions. The XRD of solid dispersions exhibits peaks less than the number of peaks of Cinnarizine in their pure form. This suggests that crystallinity of both drug and

polymer is reduced in solid dispersion. Decrease in crystallinity of the drug and polymer contribute to enhancement of dissolution of the drug.

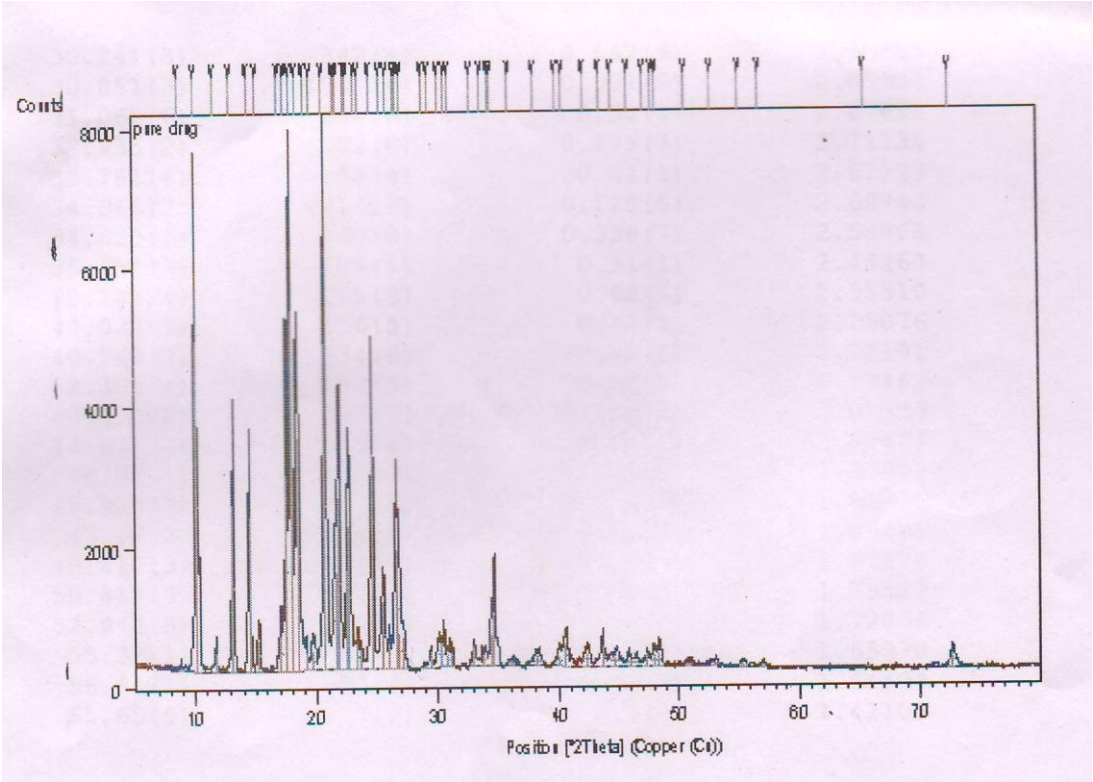


Fig3: XRD of Pure Drug

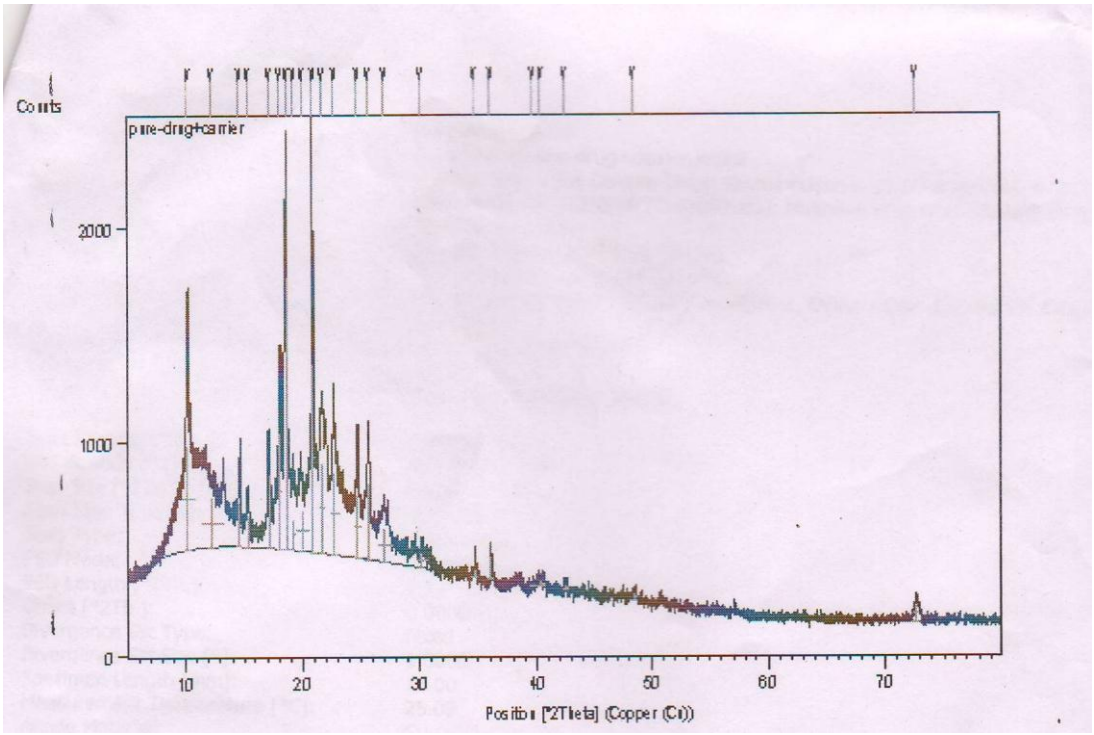


Fig4: XRD of Pure Drug+ Carrier

Table 6: Charecterization Of Pre Compression Parameters

Formulation Codes	Bulk Desnsity	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.335	0.36	6.9	1.07	17.7
F2	0.43	0.55	21.1	1.2	14.57
F3	0.231	0.296	21.9	0.78	19.3
F4	0.245	0.316	22.6	1.25	18.7
F5	0.462	0.527	12.33	0.87	20.12
F6	0.373	0.421	11.40	1.34	18.2
F7	0.56	0.69	18.84	1.25	19.93
F8	0.61	0.67	8.95	1.09	21.34
F9	0.58	0.64	9.37	0.90	23.40
F10	0.63	0.68	7.3	0.92	21.23
F11	0.52	0.56	7.14	0.92	22.03
F12	0.53	0.58	8.62	1.09	21.64
F13	0.60	0.64	6.25	1.06	20.34
F14	0.57	0.63	9.52	1.10	23.42
F15	0.59	0.68	13.23	0.86	20.21

Table 7: Characterization of Post Compression Parameters

Formulation Codes	Weight Variation (%)	Hardness(kg/cm^2)	Thickness(µm)	Friability (%)
F1	6.62	2.3±0.2	3.27	0.2
F2	4.5	2.8±0.2	3.2	0.1
F3	3.1	2.8±0.2	3.4	0.1
F4	4.8	2.8±0.2	3.47	0.7
F5	3.6	3.4±0.2	3.51	0.4
F6	5.2	3.2±0.3	3.32	0.1
F7	2.4	2.8±0.1	3.1	0.6
F8	3.7	2.8±0.2	3.3	0.7
F9	5.07	2.3±0.2	2.93	0.4
F10	6.1	2.6±0.5	3.21	0.6
F11	3.52	2.7±0.2	3.03	0.2
F12	5.2	2.6±0.2	3.07	0.4
F13	4.9	2.6±0.2	3.01	0.2
F14	4.2	2.3±0.2	3.3	0.3
F15	2.8	2.3±0.3	3.2	0.4

Table 8: Characterization of Post Compression Parameters

Formulation Codes	Disintegration Time (Sec)	Wetting Time (Sec.)	Drug Content (%)
F1	42	39	89.27
F2	53	42	89.8
F3	52	32	83.6
F4	42	46	99.2
F5	53	38	73.9
F6	41	35	93.7

F7	52	33	86.88
F8	43	40	89.2
F9	40	38	79.6
F10	29	31	82.3
F11	24	36	88.98
F12	27	33	86.6
F13	24	34	87.71
F14	23	32	87.2
F15	22	31	79.9

Table 9: Dissolution profile

Time	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
0	0	0	0	0	0	0	0
4	39.77	13.6	27.4	19.25	15.24	15.06	21.703
8	59.89	22.69	46.44	40.50	37.88	27.35	31.98
12	63.06	39.53	76.57	48.79	45.94	54.65	55.62
16	68.73	52.39	88.56	63.21	66.81	73.13	58.93
20	89.35	79.91	98.26	75.10	92.42	79.08	69.21

Table 10: Dissolution profile

Time	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**
0	0	0	0	0	0	0	0	0
4	9.19	30.08	17.36	16.31	11.43	3.24	14.74	28.78
8	31.42	51.65	28.46	32.10	27.21	17.10	42.44	83.88
12	55.62	72.17	39.96	42.31	42.12	44.94	61.01	91.94
16	58.93	87.26	52.94	67.21	66.21	67.28	62.69	94.65
20	69.21	88.48	72.50	88.9	86.6	92.01	64.27	98.80

Table 11: Factorial Design Layout for Crospovidone and SSG:

Batch Code	**Variable Level in Coded Form**		**D.T.**	**Friability**	**% Drug Release**
	X1	X2			
F7	0	0	24	0.2	88.9
F8	-1	1	24	0.2	90.017
F9	1	-1	40	0.4	88.48
F10	0	-1	43	0.7	69.2
F11	-1	-1	52	0.6	81.59
F12	1	0	27	0.4	86.6
F13	1	1	22	0.4	98.8
F14	0	1	23	0.3	64.27
F15	-1	0	29	0.6	72.5

Coded Values	Actual Values	
	X1(%W/W)	X2(%w/w)
-1	2	2
0	4	4
+1	6	6

Table 12 Constraints

CONSTRAINTS			
Name	**Goal**	**Lower Limit**	**Upper Limit**
Crospovidone	Is in range	-1	+1
SSG	Is in range	-1	+1
DT(Sec.)	Target=27.45	22	52
Friability(%)	Target=0.45	0.2	0.7
% Drug Release	Target=82.26	64.27	98.8

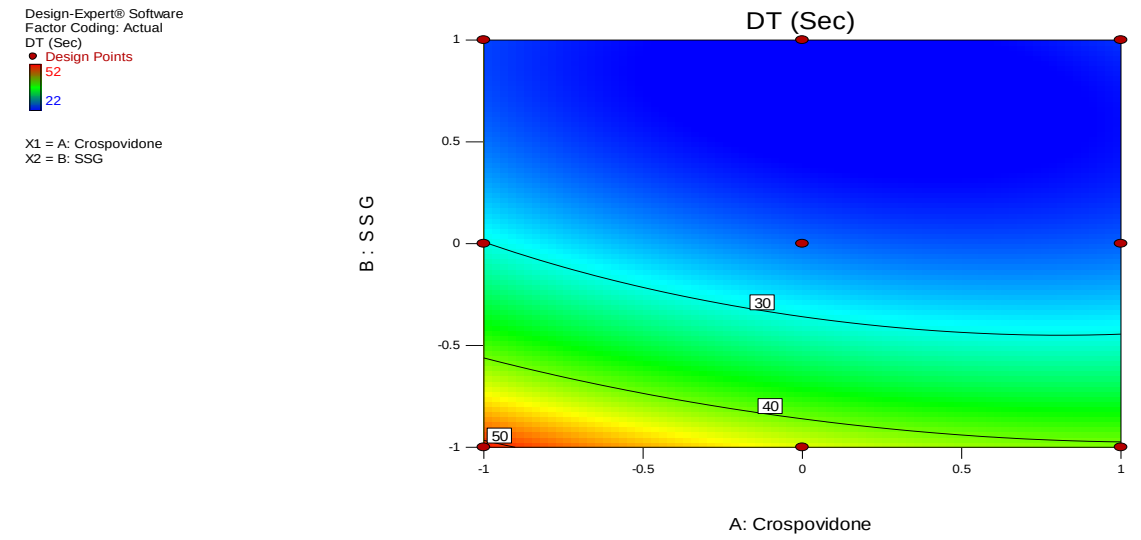
Table 13: SOLUTION

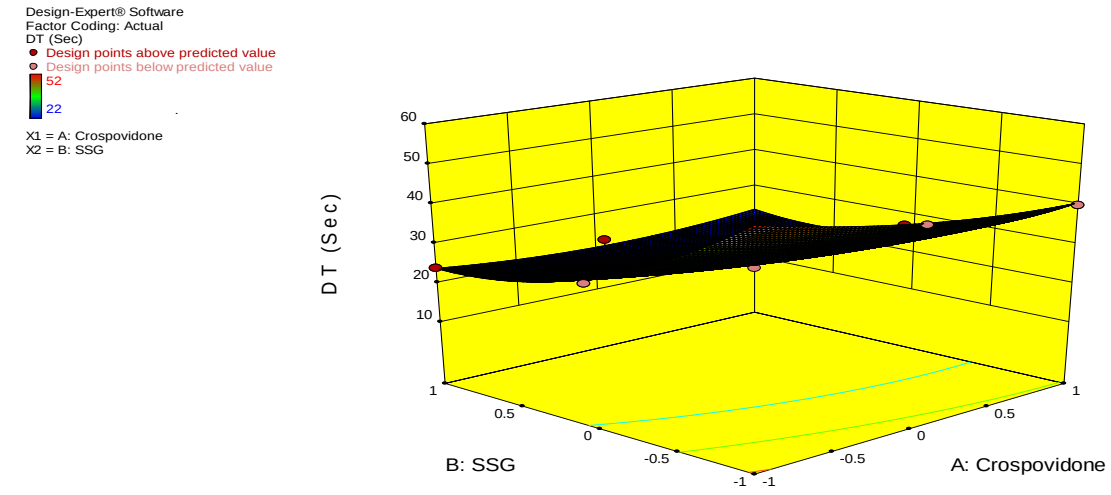
Crospovidone X1	SSG X2	D.T. (sec)	Friability(%)	Drug Release (%)	Desirability
0.221	0.131	27.45	0.45	82.26	0.90

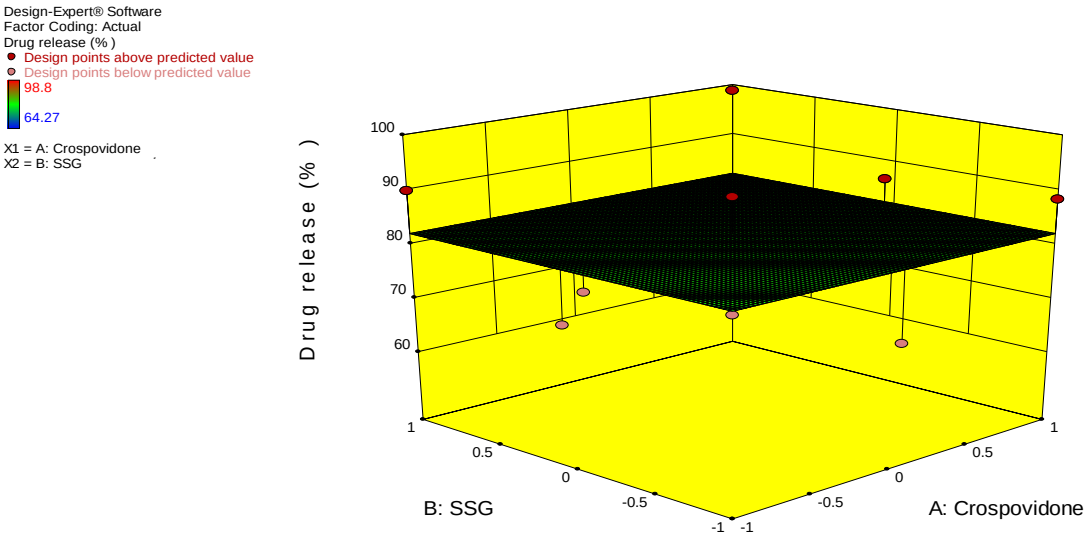
Response Surface plot

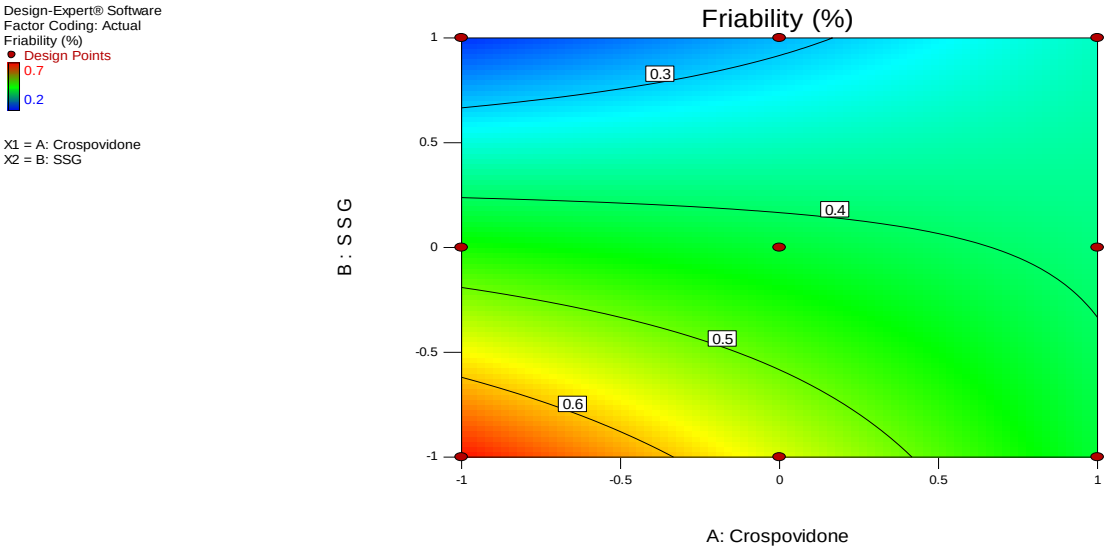
Response surface plots were generated for each response to study the effect of each factor and the behavior of the system.

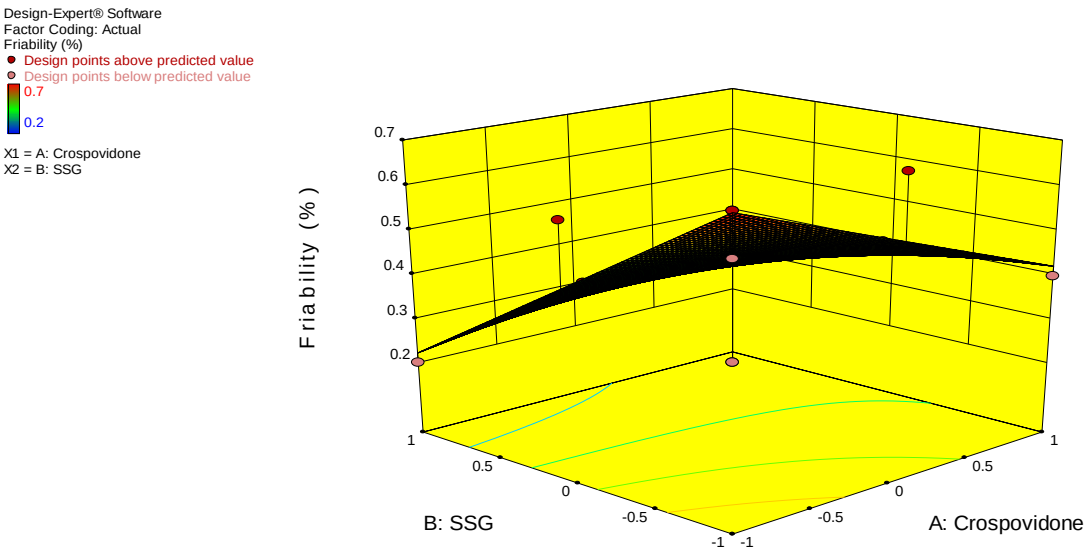
dsfCC






Design-Expert® Software
Factor Coding: Actual
Drug release (%)
Design points above predicted value
Design points below predicted value
98.8
64.27
X1 = A: Crospovidone
X2 = B: SSG
Drug release (%)
100
90
80
70
60
1
0.5
0
-0.5
-1
B: SSG
A: Crospovidone


Design-Expert® Software
Factor Coding: Actual
Friability (%)
Design Points
0.7
0.2
X1 = A: Crospovidone
X2 = B: SSG
Friability (%)
B: SSG
A: Crospovidone
0.3
0.4
0.5
0.6


Design-Expert® Software
Factor Coding: Actual
Friability (%)
Design points above predicted value
Design points below predicted value
0.7
0.2
X1 = A: Crospovidone
X2 = B: SSG
Friability (%)
0.7
0.6
0.5
0.4
0.3
0.2
B: SSG
A: Crospovidone

Optimum Formulation

A 3^2 full factorial design was used in the present study. In this deign 2 factors were evaluated, each at 3 levels, and experimental trials were performed at all 9 possible combinations. The amount of superdisintegrant, Crospovidone and SSG were selected as independent variables. The disintegration time, percent friability and percent drug release were selected as dependent variables. In order to investigate the factors systematically, a factorial design was employed in the present investigation. Formulation optimization has been done by using 3^2 full factorial design, preparing nine batches of formulations (F7 to F15). A polynomial equation was derived for in vitro dispersion time, by backward stepwise linear regression analysis, using Design expert 9 software. Formulation containing 2.42mg w/w Crospovidone, and 2.26 mg w/w Sodium Starch Glycolate was found to be promising with an in vitro dispersion time of 29 sec, friability of 0.42% and percent drug release 80.5%.

Optimum Formulation for Mouth Dissolving Tablet of Cinnarizine

The optimization formulation was prepared with best concentration of crospovidone and SSG. The optimized tablets were prepared and characterized for their physiochemical properties.

Table 14 Formula of Optimized Formulation

INGREDIENTS	QUANTITY PER TABLET(mg)
Solid Dispersion	60
Crospovidone	2.42
SSG	2.26
Sodium Bicarbonate	2
Citric Acid	5
Aspartame	3
Mannitol	10
Magnesium Stearate	2
Microcrystalline Cellulose	12.66

Table 15: Results of optimum formulation:

S.No	Parameter	Result
	Precompression Parameters	
1.	Bulk Density	0.57
2.	Tapped Density	0.63
3.	Compressibility Index	9.52
4.	Hausner's Ratio	1.10
5.	Angle of repose	22.2
	Post compression Parameters	

1.	Weight Variation	3.9%
2.	Thickness	3.3µm
3.	Hardness	2.3±0.2kg/cm^2
4.	Friability	0.42%
5.	Disintegration Time	29 Sec
6.	Wetting Time	42 Sec
7.	Drug Content	89.7%
8.	Percent Drug Release	80.5%

DISCUSSION

The solubility was obtained from a SD containing CINNARIZINE: PVP K30 of 1:3 w/w prepared by kneading method. Solid dispersion technique by kneading method used for solubility enhancement of water insoluble drug showed better results for enhancement of solubility.PVP K30 was used as carrier for solubility enhancement. Most solubility was obtained from a SD containing CINNARIZINE: PVP K30 of 1:3 w/w prepared by kneading method SSG and crospovidone as superdisintegrants had effect on the disintegration time as its concentration was increased from F1 to F15. The disintegration time of F2, F3, F5, F7, F12 was increased due to increase in increase in concentration of superdisintegratnts. It may be due to capillary action or swelling action. Pre-compression results showed the better flow properties of powder blend showed in Table. The drug content of all the formulations was found to be between 73.9-99.2%. Tablets with lower friability may not break during handling on machines. In-vitro release studies were carried out using tablet dissolution test apparatus paddle method at 37±0.5 °C, taking 900 ml of 0.1N HCl as dissolution medium. Speed of rotation of the paddle was set at 50 rpm. Aliquots of 5 ml were withdrawn after 4,8,12,16 and20 min and analyzed spectrophotometrically at 253 nm. Formulation F15 prepared by direct compression showed release 98.80% drug at the end of 20 min. The rapid drug dissolution might be due to easy breakdown of particles due to SSG and crospovidone and rapid absorption of drugs into the dissolution medium. The optimized formulation was prepared by applying the formula according to design expert 9.1 software and was evaluated for all the precompression and post compression parameters. The results of optimized formulation was approximately same as accepted results according to software design expert 9.1.Thus, it can be concluded that combination of solid dispersion and super disintegrants is a promising approach to prepare efficient mouth dissolving tablet of poorly water soluble drug i.e. Cinnarizine.

CONCLUSION

On the basis of obtained results it can be concluded that the solubility of cinnarizine was increased by solid dispersion technique using PVP K30 as carrier. Formulation of MDT by using SD of Cinnarizine is unique technique by which solubility of the drug can be enhanced which is most challenging aspect of drug delivery. The technique adopted was found to be economical and industrially feasible. Thus, it can be concluded that combination of solid dispersion and super disintegrants is a promising approach to prepare efficient mouth dissolving tablet of poorly water soluble drug i.e. Cinnarizine.

REFERENCES

1. Chein YW. Oral Drug Delivery systems. 2nd ed., New York, Marcel Dekker. 1992; 5(2): 19-20.
2. Aggarwal S., Gupta G. D. Chaudhary S. Solid dispersion as an eminent strategic approach in solubility enhancement of poorly soluble drugs. International Journal of Pharmaceutical Sciences and Research, 2010; 1(8): 1-13
3. Bhowmik D, Chiranjib B, Krishnakanth, pankaj, Chandira MR. fast dissolving tablet, Journal of Chemical and Pharmaceutical Research. 2009; 163-177.
4. Guerin E, Tchoreloff P, Leclerc B, Tanguy D, Deleuil M, Couarraze G. Rheological characterization of pharmaceutical powders using tap testing, shear cell and mercury porosimeter. International Journal of Pharmaceutics.1999; 91-103.
5. Gupta A, Mishra KA, Gupta V, Bansal P, singh R, singh KA. Recent trends of fast dissolving tablets: An overview of formulation technology. International Journal of Pharmaceutical Research and Bio-Science.2010.
6. Dhakane K, Rajebahadur M, Gorde P, Salve P. Fast dissolving tablet: A future prospective. Journal of Pharmacy Research. 2011; 4176-4180.
7. Sandeep N, Gupta MM. Immediate drug release dosage form: A review: Journal of Drug Delivery & Therapeutics. 2013; 55-161.
8. Manikandan M, Kannan K, Thirumurugu S, Manavalan R. Research Journal of Pharmaceutical, Biological and Chemical Sciences: 2012; 425-434.
9. Banker GS, Anderson NR, Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. New Delhi: CBS publishers & distributors; 2009; 3rd edition, 293-345.
10. Cooper J, Gunn C, carter SJ; Tutorial Pharmacy. CBS Publishers and Distributors. New Delhi, India, 1986; 211-233.

11. International Convention for Pharmaceutical Industry. ICH Guidelines on Analytical Method Validation. 2005.
12. Abo E. Development and Evaluation of Fast Disintegrating Extended Release Tablets Containing Antihypertensive Drug. International Journal of Pharmacy and Pharmaceutical Sciences. 2014; 6(6): 165-174.
13. Garrett ER, Carper.JRF. Am. Pharm. Asso. Sci. 1955; 44: 515.