RESEARCH PAPER

Development and Optimization of Cinnarizine & Dimenhydrinate Mdts: A Solid Dispersion Approach for Solubility Enhancement

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Received: 16th Dec, 2025; Revised: 8th Feb 2026; Accepted: 12th Feb, 2026; Available Online: 28th Feb, 2026

ABSTRACT
Introduction: By generating a high-energy, metastable system that enhances surface area and encourages amorphization, the solid dispersion technique has become a reliable and adaptable method for accelerating the pace at which hydrophobic medications dissolve. Objective: To develop and optimize an MDT formulation using solid dispersion and co-processed superdisintegrants (Sodium Starch Glycolate and Crospovidone) to ensure rapid disintegration and maximum drug release. Methods: The formulation strategy employed a two-step enhancement process: first, the creation of Cinnarizine solid dispersions using thermal fusion, and second, the development of an ultra-fast disintegrating core. By employing co-processed superdisintegrants, the study leveraged the combined strengths of SSG and CP. To ensure an optimized final product, a factorial design (32) was implemented to map the complex interactions between excipient concentrations and disintegration efficiency. Results: Excellent pharmaceutical qualities were demonstrated by the manufactured optimized tablet (OPT FKL). Extremely fast disintegration—25–28 seconds—is essential for a prompt start to action. In under 15 minutes, 90.7% of the drug (cinnarizine) and 97.4% of the drug (dimenhydrinate) were released, considerably outperforming the pure medicines and achieving the goal of quick drug availability. Conclusion: This study offers a potent two-pronged formulation strategy: first, the solid dispersion technique effectively overcame the solubility limitation of the drugs (especially Cinnarizine); second, the engineered fast-disintegrating tablet platform ensured the rapid release and presentation of the dissolved drug for absorption.
Keywords: Cinnarizine, Dimenhydrinate, MDTs, superdisintegrants , SSG, Crospovidone
How to cite this article: Choudhary NK, Mittal N, Development and Optimization of Cinnarizine & Dimenhydrinate Mdts: A Solid Dispersion Approach For Solubility Enhancement. Int J Drug Deliv Technol. 2026;16(18s): 1013-1023. DOI: 10.25258/ijddt.16.18s.114
Source of support: Nil.
Conflict of interest: None

1. INTRODUCTION

Oral administration remains the most desirable and favored mode for therapeutic medicines due to high patient compliance, ease of intake, and cost-effective manufacturing. [1, 2] With the rising costs of developing new chemical entities, the pharmaceutical industry has pivoted toward innovating drug delivery systems (DDS) for existing medications to enhance their efficacy and bioavailability.[3, 4] A significant obstruction in drug formulation is the stagnant dissolution rate of hydrophobic compounds, which severely compromises their systemic absorption. Cinnarizine and Dimenhydrinate both critical anti-emetics fall into BCS Class II, meaning their therapeutic potential is hindered by poor aqueous solubility. To ensure consistent clinical outcomes and reliable bioavailability, it is imperative to implement advanced solubility-enhancing strategies to overcome this inherent dissolution barriers.[5-6]

Among the methods used to increase the solubility of medications that are poorly soluble in water include micronization, amorphous drug manufacture, and the formation of solid dispersions with hydrophilic carriers.[1, 7] Solid dispersions are groups of solid goods made up of two or more distinct elements, frequently a hydrophobic drug and a hydrophilic matrix. In aqueous solutions, pharmaceuticals that are insoluble in water dissolve their carriers, releasing the drug as tiny colloidal particles. Solid dispersion methods can thereby increase the drug's bioavailability and dissolve it more quickly.[8–9]

By producing a high-energy, metastable system that increases surface area and encourages amorphization, the solid dispersion approach has evolved into a reliable and adaptable method to increase the dissolving rate of such hydrophobic drugs. [10] A possible synergistic approach is created by the development of fast-disintegrating tablets (FDTs), which offer the benefits of rapid disintegration without water and improved patient compliance—particularly helpful for those who feel queasy or vomiting. [11–12] Using orodispersible tablets (ODTs), a newly developed drug delivery technique, is an innovative way to increase marketing and extend patency. [13] It has been demonstrated that orodispersible dosage formulations are

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effective in treating pain, inflammation, migraines, and nausea. Numerous techniques have been demonstrated to enhance the dissolving properties of poorly soluble medications and boost bioavailability following oral absorption, and there are useful research articles available for the development of ODT.[14-15]

Using a DoE for optimization allows for a scientific understanding of the relationship between the superdisintegrant variables and the tablet's critical properties, leading to a robust and well-characterized final product. The current study aims to develop fast dissolving tablets made of solid dispersions in order to avoid dosage form-related factors (formulation factors like solubility, disintegration, and dissolution) and to improve the aqueous solubility of poorly soluble drugs like Cinnarizine and Dimenhydrinate through the use of solid dispersion technology. The general aim of the study was focused on increasing the dissolution rate of poorly soluble drugs Cinnarizine and Dimenhydrinate by formulating them into fast dissolving tablets. [16]

2. MATERIALS AND METHODS:

2.1. Materials

A free sample of drugs API was acquired from M/s Mylan Lab Pvt. Ltd. in Hyderabad. S.D. Fine Chem. Ltd. in Mumbai supplied the sodium starch glycolate (SSG) and crospovidone (CP), while Merck Pvt. Ltd. in Mumbai supplied Avicel, magnesium stearate, mannitol, and talc.

2.2. Methods

2.2.1 Formulation of Solid Dispersion

Solid dispersions (SDs) of the medication cinnarizine were created using the fusion process at four mass ratios: 1:1, 1:2, 1:3, and 1:4. In a porcelain dish, PEG-6000 and PVP-K30 polymers were heated to a maximum temperature of 165°C in order to melt them. After adding an appropriate amount of the drug to the molten mixture, it was constantly stirred until a uniform dispersion was obtained.

2.2.2 Preformulation Studies

Preparation of the Blend

Mannitol and Solid Dispersion were run through sieve #60. Sieve #20 was used for Avicel, while sieve #80 was used for all other ingredients. A polybag was used to mix the ingredients.

Evaluation of Blend:

Pre-Compression Studies[17-20]

Prior to compression, the powder mixes were assessed for adequate flow characteristics using a number of characteristic metrics, including bulk density, tapped density, compressibility index, and angle of repose.

Bulk Density: Transfer the blend into a graduated cylinder allowed for determination of the apparent BD (ρb) for each blend. The BD was calculated using below Eq:

$\rho_b = \frac{M}{Vb}$ Where V_b is bulk volume and M is weight of powder

Tapped Density:

The blend's weight (M) and the cylinder's constant minimum volume (Vt) were measured after tappings. The tapped density (ρ_t) was calculated using the formula as shown in below Eq.

$\rho t = M/Vt$

Compressibility Index: The easiest approach to gauge a powder's flow is to look at its compressibility, which is a measure of how easily a powder can flow.

$I = (\rho t - \rho b)/(\rho t) \times 100$

Angle of Repose

A vertically adjustable funnel was used to pour the powder mixture onto paper until the desired cone height (h) was reached. The formula displayed allowed for the calculation of the angle of repose (θ) and the measurement of the heap's radius (r): $\tan \theta = h/r$

Hausner's Ratio: An indirect measure of powder flow easiness is the Hausner ratio. Blend characterisation is a crucial component that provides insight into the final preparation's features. Compressibility influences the tablet's size, hardness, and subsequent disintegration and release.

Hausner ratio = ρ_t / ρ_b

2.2.3 Formulation and Optimization of Drug MDTs [21-22]

Preparation of physical mixture and co-processed superdisintegrants: The physical mixture of sodium starch glycolate and crospovidone was prepared by mixing them together in glass pestle motor. The co-processed super-disintegrant was prepared as follows:

Lyophilized Technology: A total of 50 mL of water was combined with 10 g of SSG and CP blends at various ratios. Each mixture was placed in a round-bottom flask (RBF) and frozen until solid, using a condenser set to -77.5 °C (Table 1). The frozen samples were then lyophilized under vacuum (0.02 mbar) for four hours, allowing complete water sublimation. The resulting dry powder was stored in a desiccator.

Preparation of Drug MDT's:

The 200 & 250 mg, flat-faced, 5 mm-diameter tablets were produced using a single punch tablet machine. MDT formulations, each weighing 250 mg, were made by combining a mixture of sodium starch glycolate and crospovidone with solid dispersions of cinnarzine (equivalent to 60 mg in each tablet) and dimenhydrinate (40 mg) at varying concentrations (2% to 6%), as these super-disintegrants function best in the range of 2% to 8% (Table 2). Super-disintegrants were combined to make batches. [21-22]

Table 1: Composition of MDT with Physical Mixture and Coprocessed Superdisintegrants (Preliminary Batches)

Formulation	F1*	F2+	F3#	F4	FP5*	FP6+	FP7#	FP8	FK9*	FK10+	FK11#	FK12
Cinnarizine	20	20	20	20	-	-	-	-	-	-	-	-
Dimen	40	40	40	40	40	40	40	40	40	40	40	40
Drug CSD 1:3	-	-	-	-	60	60	60	60	60	60	60	60
SSG	2	2	2	-	2.5	2.5	2.5	-	2.5	2.5	2.5	-
Crospovidone	2	2	2	-	2.5	2.5	2.5	-	2.5	2.5	2.5	-
Avicel PH 102	40	40	40	40	50	50	50	50	50	50	50	50
Mannitol	40	40	40	40	50	50	50	50	50	50	50	50
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mg. Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Lactose (QS)	100	100	100	100	250	250	250	250	250	250	250	250
	Total weight 200mg				Total weight 250mg							

Table 2: Formulation of Factorial Design Batches of PVP K-30 SD of drug (Lyophilized Technology)

Ingredients	FKL1	FKL2	FKL3	FKL4	FKL5	FKL6	FKL7	FKL8	FKL9
Cinnarzine SD	60	60	60	60	60	60	60	60	60
Dimen	40	40	40	40	40	40	40	40	40
SSG	2.5	2.5	2.5	5	5	5	7.5	7.5	7.5
Crospovidone	2.5	5	7.5	2.5	5	7.5	2.5	5	7.5
Avicel PH 102	50	50	50	50	50	50	50	50	50
Mannitol 20%	50	50	50	50	50	50	50	50	50
Talc 5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mg. stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Lactose (qs)	250	250	250	250	250	250	250	250	250
Superdisint. %	2	3	4	3	4	5	4	5	6

FKL- **F**actorial Batch of PVP **K**-30 SD prepared by **L**yophilized Technology

2.2.4 Optimization of factorial batches MDTs of PVP K-30 prepared by Lyophilized Technology:

In order to reduce Disintegration Time (DT) and optimize Drug Release for two drugs Cinnarizine (Cinn) and Dimen-hydrinate (Dimen)—the study seeks to determine the ideal levels of two formulation variables (X1 and X2, likely quantities of excipients such a super-disintegrant). to determine the best mix of two super-disintegrants in order to develop a fast-dissolving tablet formulation that contains two poorly soluble medications (dimen and cinn).

Evaluation of Compressed Tablets [23-26]

a. General Appearance

This includes tablet's size, shape, color, presence or absence of an odor, taste, surface texture.

b. Tablet Thickness: Ten tablets from each batch were taken and their thickness was recorded using Eureka Thickness Tester. The data is shown in Table 7A.

c. Hardness

Each batch's ODT hardness was assessed using a Monsanto hardness tester. It is expressed in kg/cm2. The hardness of three randomly selected tablets from each formulation was measured. Table 7A displays the data.

d. Weight Variation: According to IP, a weight variation test was performed on each batch of ODTs that were made. Twenty tablets were ingested and weighed separately; the average weight was computed and compared to the weight of each individual tablet to determine any changes.

e. Friability: The Roche friabilator was used to assess the tablets' friability. Twenty pre-weighed MDT

samples were put in a plastic chambered friabilator that was connected to a motor that rotated at 25 rpm for four minutes. After dusting and reweighing the tablets, the percentage of friability was determined.

f. Wetting Time: A 10-cm-diameter petri dish was filled with five circular tissue papers. The petridish was filled with ten milliliters of phosphate buffer pH 6.8 that included amaranth, a water-soluble color. To determine if the tablet surface was completely moist, the dye solution was utilized.

***g. In-vitro* Disintegration Test**

The action of saliva causes fast-disintegrating tablets to dissolve in the mouth; nevertheless, the amount of saliva in the mouth is restricted, and no tablet disintegration test was discovered in USP and IP to replicate in vivo conditions. Six milliliters of water were added to the vessel so that two milliliters were above the sieve and four milliliters of the media were below it in order to measure the disintegration time. After setting the tablet on the filter, the assembly was put on a shaker. The tablet's disintegration time was determined by measuring how long it took for every particle to pass through the sieve.

h. Content Uniformity:

In a different volumetric flask, an aliquot of 2.5 ml of the stock solution was diluted to 10 ml using phosphate buffer pH 6.8. The above sample's absorbance was measured spectrophotometrically at 257 nm, and a calibration curve was used to quantify its concentration.

% Drug Content = Sample Absorbance/ Standard Absorbance x 100

***i. In vitro* Release study:**

The tablets were put in a dissolution tank with 900 cc of pH 6.8 phosphate buffer, kept at 37ºC ± 0.5, and agitated at 50 rpm. Samples (6 ml) were taken at various intervals (1, 2, 4, 6, 8, 10, 15 min) and replaced with new dissolving medium. At 257 nm, the absorbance was measured using spectrophotometry.

3. RESULTS AND DISCUSSION

3.1 Characterization of Solid Dispersions

The drug content in each solid dispersion was ascertained using the UV-spectroscopic method; the results are shown in table 3. The drug concentration of cinnarizine solid dispersions was reported to range from 96.85% to 99.65%.

Table 3: Drug Content in Cinnarizine Solid Dispersion

Formulation code of Solid dispersion (with PEG)	Drug content (%) n=3	Formulation code of Solid dispersion (with PVP K30)	Drug content (%) n=3
CSD P11	96.85 ± 1.86	CSD K11	98.25 ± 1.13
CSD P12	98.78 ± 1.25	CSD K12	98.72 ± 1.26
CSD P13	99.25 ± 1.18	CSD K13	99.65 ± 1.54
CSD P14	99.28 ± 1.35	CSD K14	99.4 ± 1.08

3.2 Solubility studies: The aqueous solubility of the Cinnarizine in presence of selected polymers taken in varying ratios increased linearly with polymer concentration. It was also observed that after increasing in concentration of polymers from 1:3 to 1:4 of Cinnarizine there was no significant increase in solubility of Solid dispersions (Table 4).

Table 4: Effect of Polymer concentration on solubility of Cinnarizine

S. No.	Cinnarizine PEG/ PVP	Amount of Cinnarizine dissolved (mg/ml) at 25˚C (n=3)	
		PEG 6000	PVP K30
1	1:0 (Pure Drug)	0.052±0.02	0.052±0.01
2	1:1	0.115±0.01	0.124±0.01
3	1:2	0.212±0.01	0.235±0.02
4	1:3	0.319±0.02	0.341±0.01
5	1:4	0.325±0.01	0.351±0.01

3.3 *In vitro* drug release of SD: It was discovered that solid dispersion formulations of cinnarizine improved the drug's solubility. The amount of the polymer (PEG 6000, polyvinylpyrrolidone (PVP)) utilized was found to affect the enhancement. In drug to polymer ratios of 1:1, Q30 (amount of drug released in 30 minutes) was found to be in the range of 78–80%, but in ratios of 1:2, 1:3, and 1:4, it was found to be 85–88%, 93–96%, and 93–96%, respectively, compared to 51% in the case of pure cinnarizine (Table 5). When the drug to polymer ratio was raised from 1:3 to 1:4, there was no discernible increase in the dissolution of cinnarizine.

Table 5: *In vitro* dissolution of pure Cinnarizine & its SD in HCl buffer pH 1.2

Formulation Code	PERCENT DRUG RELEASED AT DIFFERENT TIME INTERVALS					
	5 min	10 min	15 min	20 min	25 min	30 min
Pure Cinn	15.58±0.85	24.13±1.10	33.52±1.22	42.36±1.2	48.18±1.08	51.00±1.02
CSD P11	20.45±1.1	35.45±1.05	46.36±1.0	51.75±1.15	68.78±1.12	78.56±1.25
CSD P12	24.78±1.26	38.22±1.68	50.85±1.8	62.24±1.48	72.75±1.68	85.96±1.24
CSD P13	28.12±1.21	42.45±1.12	54.59±1.45	66.46±0.65	80.12±0.8	93.58±1.24

CSD P14	28.75±0.45	43.78±0.78	54.5±1.12	66.85±1.28	82.35±1.75	94.12±2.15
CSD K11	23.26±0.85	38.98±1.02	49.8±0.8	57.45±1.45	71.65±0.86	80.12±1.25
CSD K12	27.41±1.32	41.87±1.2	53.32±0.75	66.86±1.36	76.85±0.8	88.65±1.22
CSD K13	31.5±0.65	45.38±1.11	57.85±0.75	71.58±1.05	84.2±2.28	96.15±2.65
CSD K14	32.2±0.5	46.1±0.58	58.25±1.16	72.5±0.86	86.65±1.65	96.42±2.22

3.4 Pre-Compression Studies: Evaluation of Powder Blends:

Table 6: Characterization of powder blends

Form. Code	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Compressibility Index (%)	Angle of Repose (˚)	Hausner's ratio
F1*	0.478	0.528	9.47	21.41	1.10
F2+	0.496	0.568	12.50	20.12	1.14
F3#	0.462	0.512	9.77	21.07	1.11
F4	0.554	0.604	8.28	22.95	1.09
FP5*	0.451	0.501	9.98	21.32	1.11
FP6+	0.524	0.544	10.94	22.86	1.12
FP7#	0.438	0.488	10.25	20.48	1.11
FP8	0.496	0.546	9.16	19.36	1.10
FK9*	0.478	0.528	9.47	21.07	1.10
FK10+	0.484	0.55	10.61	22.9	1.12
FK11#	0.442	0.492	10.16	19.62	1.11
FK12	0.413	0.463	10.80	22.57	1.12

3.5 Formulation & evaluation of preliminary batches MDTs:

Table 7A: Evaluation of Preliminary Batches-1

Form. Code	Uniformity of Thickness (mm) (n =10)	Diameter (mm) (n = 3)	Hardness (kg/cm^2) (n=3)	Friability % (n=20)
F1*	3.04 ± 0.02	7.02 ± 0.01	3.69 ± 0.03	0.52 ± 0.02
F2+	3.02 ± 0.01	7.05 ± 0.02	3.35 ± 0.03	0.31 ± 0.01
F3#	3.03 ± 0.01	7.00 ± 0.01	3.47 ± 0.01	0.34 ± 0.02
F4	3.01 ± 0.03	7.04 ± 0.01	3.53 ± 0.03	0.26 ± 0.01
FP5*	3.51 ± 0.02	8.02 ± 0.01	3.39 ± 0.01	0.48 ± 0.01
FP6+	3.50 ± 0.06	8.03 ± 0.02	3.45 ± 0.04	0.32 ± 0.02
FP7#	3.52 ± 0.04	8.03 ± 0.03	3.33 ± 0.03	0.33 ± 0.03
FP8	3.53 ± 0.02	8.04 ± 0.01	3.63 ± 0.03	0.24 ± 0.01
FK9*	3.55 ± 0.01	8.01 ± 0.03	3.51 ± 0.03	0.36 ± 0.02
FK10+	3.54 ± 0.02	8.02 ± 0.01	3.59 ± 0.03	0.42 ± 0.01
FK11#	3.52 ± 0.01	8.05 ± 0.02	3.15 ± 0.03	0.50 ± 0.01
FK12	3.53 ± 0.01	8.00 ± 0.01	3.37 ± 0.01	0.37 ± 0.02

* physical mixture, + microwave technique, # indicates lyophilized technique

Table 7B: Evaluation of Preliminary Batches-2

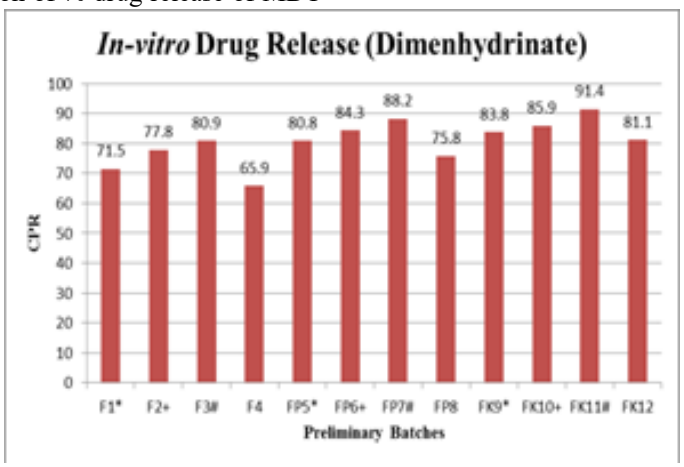
Form. Code	Weight Variation(mg) (n = 20)	Wetting time (s) (n=5)	*In-vitro* Disintegration time (sec)
F1*	202 ± 3.34	40-44	51 ± 2.24
F2+	198 ± 2.60	41-45	47 ± 1.22
F3#	203 ± 3.70	39-42	45 ± 2.78
F4	202 ± 2.95	90-94	90 ± 2.78
FP5*	251 ± 3.67	40-44	43 ± 2.41
FP6+	250 ± 3.12	35-39	41 ± 2.21
FP7#	248 ± 2.15	33-37	39 ± 1.22
FP8	249 ± 1.82	88-92	85 ± 2.89

FK9*	252 ± 2.16	28-32	38 ± 2.35
FK10+	250 ± 2.45	26-30	35 ± 2.38
FK11#	251 ± 2.12	40-44	33 ± 2.4
FK12	250 ± 2.70	85-90	76 ± 2.43

Table 7C: Evaluation of Preliminary Batches-3

Form. Code	Drug Content Uniformity Cinn(n = 10) (%)	Drug Content Dimen (n = 10) (%)	*In-vitro* Drug Release cinnarzine	*In-vitro* Drug Release dimen-hydrinate
F1*	99.56 ± 0.15	99.72 ± 0.63	65.9	71.5
F2+	97.71 ± 0.22	98.87 ± 0.72	72.2	77.8
F3#	99.04 ± 0.13	99.2 ± 0.67	75.3	80.9
F4	98.85 ± 0.26	97.01 ± 0.66	60.3	65.9
FP5*	98.29 ± 0.18	98.45 ± 0.65	75.2	80.8
FP6+	97.62 ± 0.18	98.78 ± 0.74	78.7	84.3
FP7#	98.47 ± 0.35	98.63 ± 0.57	82.6	88.2
FP8	99.33 ± 0.22	99.49 ± 0.56	70.2	75.8
FK9*	97.24 ± 0.15	99.4 ± 0.58	78.2	83.8
FK10+	99.67 ± 0.37	97.83 ± 0.76	80.3	85.9
FK11#	97.82 ± 0.28	98.98 ± 0.65	85.8	91.4
FK12	99.15 ± 0.23	99.31 ± 0.64	75.5	81.1

Table No. 6 & 7A-7C show evaluation and data of % drug release of MDT prepared from solid dispersions of Cinnarzine SD and plain Dimenhydrinate with Polymer PEG-6000 and PVP K30 in drug to polymer ratio 1:3 and Figure No. 1 show comparison of % drug release of MDT prepared from solid dispersions of Cinnarzine and plain Dimenhydrinate with Polymer PEG-6000 and PVP K30 in drug to polymer ratio 1:3 using compressed superdistegrants and its physical mixture.



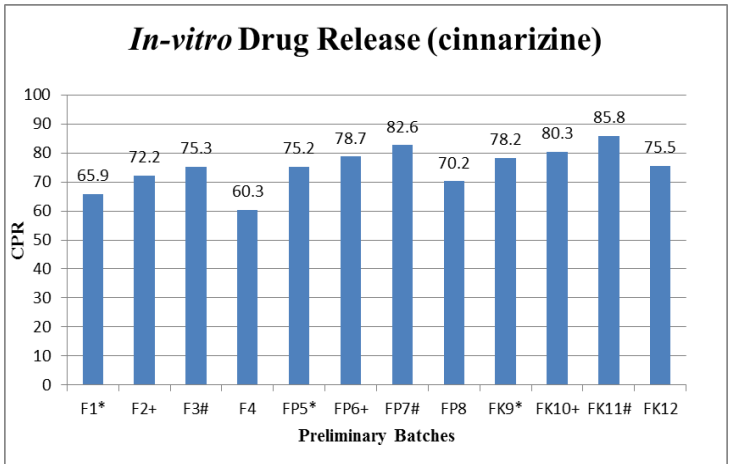


Fig 1: *In-vitro* drug release (Cinnarzine & Dimenhydrinate) of preliminary batches of MDT

DISCUSSION

In comparison to the pure drug, the formulation of Cinnarizine as a solid dispersion greatly increases its in-vitro dissolution rate, according to the findings presented. Up to a saturation point, the degree of this improvement is directly correlated with the quantity of hydrophilic polymer (PEG 6000 & PVP K30) utilized. The ideal balance of polymer-mediated solubilization and dispersion for Cinnarizine under the investigated conditions is provided by a drug-to-polymer ratio of 1:3, beyond which no additional dissolution improvement is attained. PVP K30 Polymer is used for more research based on the results.

3.6 Optimization of MDTs of factorial FKL batches:

With the aid of Design Expert® Software 11.0.4, optimization was carried out to determine the precise quantity of sodium starch glycolate (X1) and crospovidone (X2) needed for the preparation of MDTs of FKL. A randomized full factorial design was employed for nine runs to observe the impact of two independent variables at three levels on three responses, namely, disintegration time and percent drug release of drugs. The results are shown in table 8 & Fig 2.

Table 8: 3^2 Full Factorial Design Layouts (MDT of FKL)

Batch Codes	Variable Levels in Coded Form		Disintegration Time	% drug Release Cinn	% drug Release Dimen
	X_1 (SSG)	X_2 (CP)	DT (s)	Disso (%)	Disso (%)
FKL1	2.5	2.5	42	80.54	91.31
FKL2	5	2.5	41	83.7	92.17
FKL3	7.5	2.5	39	86.24	93.42
FKL4	2.5	5	38	84.52	94.65
FKL5	5	5	36	87.34	95.43
FKL6	7.5	5	33	90.12	98.11
FKL7	2.5	7.5	31	84.06	97.69
FKL8	5	7.5	28	88.65	97.2
FKL9	7.5	7.5	26	91.75	95.58
OPT	**7.5**	**7.5**	**26.55**	**91.69**	**97.9**

X_1 indicates amount of Sodium starch Glycolate (mg); X_2, amount of Crospovidone (mg)

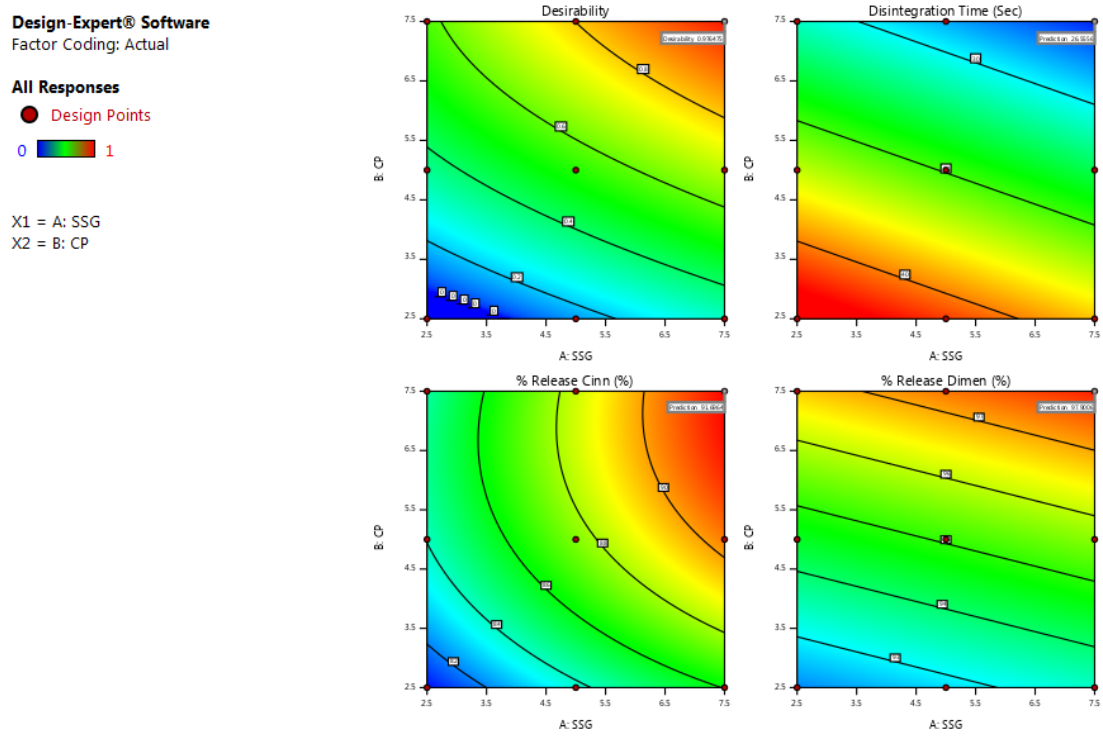


Fig. 2 Response Surface Plot for Desirability of Optimized formulation of FKL

3.6.1 Optimization of the Mouth Dissolving Tablet

The responses' disintegration time and percentage friability were linked to the transformed factor by the fitted equation. After taking into account the amount of the coefficient and the mathematical sign it conveys (i.e., positive or negative), inferences can be drawn from the polynomial equations (Table 9).

Table 9: Summary of Results of Regression Analysis

	Intercept	A	B	AB	A^2	B^2
Disintegration Time	34.8889	**-2.16667**	**-6.16667**			
p-values		**0.0009**	**< 0.0001**			
% Release Cinn	87.5656	**3.165**	**2.33**	0.4975	-0.358333	**-1.50333**
p-values		**0.0004**	**0.0010**	0.1081	0.3316	**0.0168**
% Release Dimen	95.0622	0.576667	**2.26167**			
p-values		0.3875	**0.0107**			

The optimized tablet was created by applying a full factorial design and using polynomial terms. Its goals were to reduce the disintegration time by 26 seconds, increase the drug release percentage by 91.31 percent for cinnarzine, & increase the drug release percentage by 98.11 percent for di-menhydrinate. The optimization was done with the help of software Design Expert 11.0.4. The tablet formulation (OPT), which served as the regression analysis model's checkpoint, included the optimal quantity of the co-processed sodium starch glycolate & cros-povidone (Table 10 & Fig 3)**.** The software was used to create the response surface prediction charts.

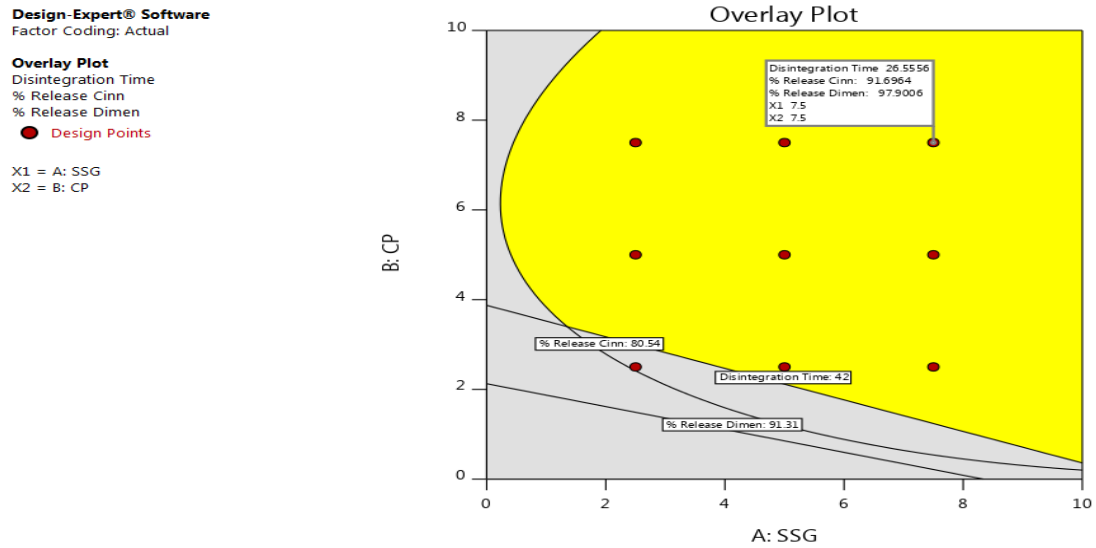


Fig. 3: Predicted Optimized FKL Formulation Overlay Plot

Table 10: Solution of Optimization of Mouth Dissolving Tablet of FKL

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
A:SSG	is in range	2.5	7.5	1	1	3
B:CP	is in range	2.5	7.5	1	1	3
DT	minimize	26	42	1	1	3
% Release Cinn	maximize	80.54	91.75	1	1	3
% Release Dimen	maximize	91.31	98.11	1	1	3
Solution						
SSG	CP	DT	% Release Cinn	% Release Dimen	Desirability	
7.5	7.5	26.55	91.69	97.90	0.976	Selected

3.6.2 Discussion:

The formulation with **SSG = 7.5** and **CP = 7.5** again proves to be optimal. It meets all five critical quality attribute (CQA) goals and achieves an exceptionally high overall desirability.

1. **Consistently Optimal Formulation**: The combination of **SSG at 7.5% and CP at 7.5%** remains the best-performing formulation, demonstrating its robustness across different target specifications or experimental runs.
2. **Outstanding Desirability**: The **Desirability Score of 0.976** indicates a nearly perfect balance. The slight

deviation from 1.000 is almost certainly due to the drug release values being *just a fraction of a percentage point below* their strict upper limits, rather than exceeding them.

3. **Performance Highlights**:

- **DT (26.55s)**: The result is outstanding. It not only meets the "minimize" goal but shatters the upper limit (42s), indicating an ultra-fast disintegrating tablet.
- **Drug Release**: Both release values (91.69% for Cinn, 97.90% for Dimen) are at the **practical maximum**, hitting the upper bounds of their specified optimal ranges. This represents a complete and rapid release profile.

The formulation with 7.5% SSG and 7.5% CP is conclusively validated as the optimal choice. It produces a **very fast-disintegrating tablet (26.55s) with maximized drug release** for both active ingredients, fully satisfying the more stringent targets set for this analysis. The high and consistent desirability score confirms that this formulation robustly delivers the desired product performance.

3.7 Development of Optimized Mouth Dissolving Tablet:

The optimal quantity of super-disintegrant recommended by the software was used to make the optimum Mouth Dissolving tablet (Table 11). The super-disintegrants both SSG and Crospovidone are required different amount for the preparation of optimized tablets of selected batch of solid dispersions of cinnarzine and dimenhydrinate.

Table 11: Development & Evaluation of Optimized Formulation

Ingredients/Formulation	OPT FKL (F1) (mg)
Cinnarizine SD	40
Dimenhydrinate	60
SSG	7.5
Crospovidone	7.5
Avicel PH 102	45
Mannitol	30
Talc	3.75
Mg. stearate	3.75
Lactose (qs)	150
Evaluation	
Weight (mg)	248 ±2.60
Hardness (kg/cm^2)	3.75 ± 0.03
Wetting time (s)	30-31
Cinnarzine Content (%)	99.42±0.2
Dimenhydrinate Content (%)	99.12±0.2
Friability (%)	0.3 ± 0.02
Disintegration time (s)	25-28
Cinnarzine release (%) Q_{15}	90.7
Dimenhydrinate release (%) Q_{15}	97.4

Table 12: Percent drug release of Optimized formulations

Time (min)	Percent Drug Release (CPR) OPT FKL (F1)	
	Cinn Release	Dimen Release
1	23.5	24.2
2	40.2	46.4
4	57.3	65.3
6	71.1	77.2
8	84.8	84.4
10	88.8	91.3
15	90.7	97.4

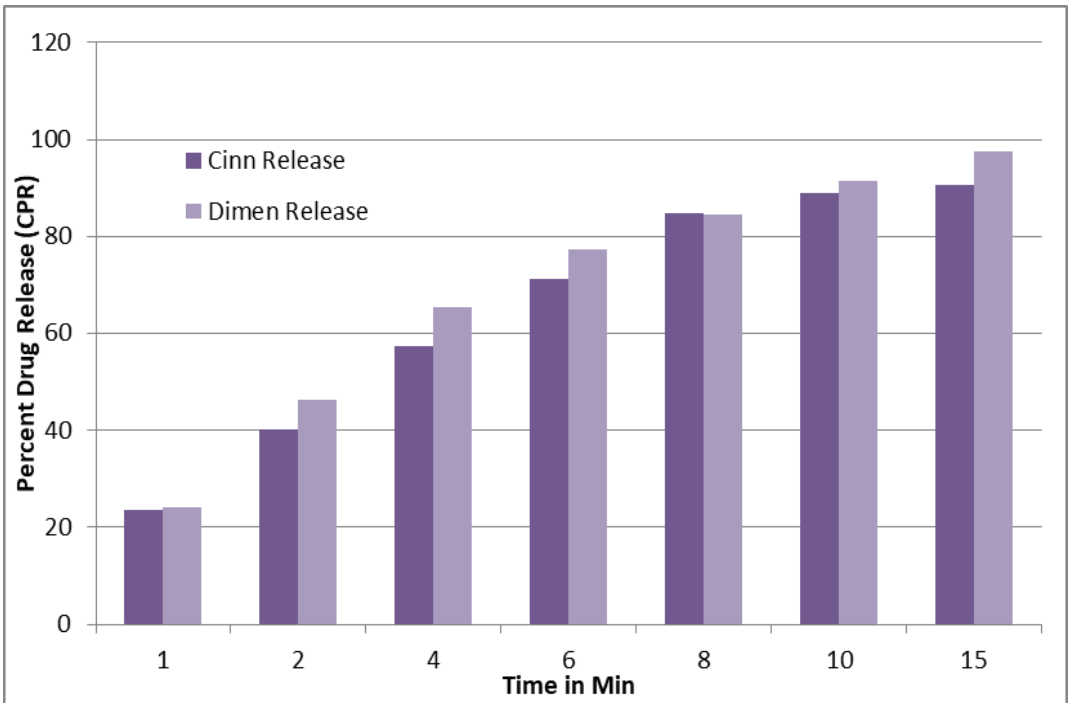


Fig. 4: Percent drug release of Optimized formulations

4. CONCLUSION

The present study successfully developed an optimized **Mouth Dissolving Tablet (MDT)** containing a combination of **Cinnarizine** and **Dimenhydrinate** using solid dispersion technology and a factorial design approach.

- Solubility Enhancement: The formulation of Cinnarizine as a solid dispersion with PVP K30 (1:3 ratio) proved to be the most effective strategy, increasing the drug's solubility and enhancing its Q_{30} release from a mere 51% to over 96%.
- Optimized Disintegration: Through a 3^2 full factorial design, the synergistic effect of Sodium Starch Glycolate (7.5 mg) and Crospovidone (7.5 mg) was validated. The optimized formulation (OPT FKL) achieved an ultra-fast disintegration time of 25–28 seconds, significantly exceeding the efficiency of traditional formulations.
- Rapid Drug Release: The final MDT demonstrated superior *in-vitro* performance, releasing 90.7% of Cinnarizine and 97.4% of Dimen within just 15 minutes, ensuring a rapid onset of action suitable for the management of motion sickness and vertigo. (Fig 4)
- Quality & Robustness: The optimized tablet maintained excellent strength (hardness of 3.75 kg/cm) and low friability (0.3%), with a high desirability score of 0.976 (Table 12).

In summary, the integration of **PVP K30-based solid dispersions** and a balanced concentration of **superdisintegrants** provide a robust platform for the delivery of poorly soluble drugs in a patient-friendly, fast-dissolving format. This optimized MDT offers a promising alternative to conventional tablets, potentially improving patient compliance and therapeutic outcomes.

ACKNOWLEDGEMENTS

Authors are thankful to the Management and Dean, faculty of Pharmacy, Lords University, Alwar, for their guidance during this work and for providing all the necessary facilities to carry out this research.

CONFLICT OF INTEREST

No conflicts of interest are mentioned by the researchers. The composition and writing of the document are the sole responsibility of the writer.

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