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Formulation and Optimization of Fast Dissolving Cinnarizine Tablets

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ABSTRACT: Cinnarizine is H1 anti histaminic and also a calcium channel blocker. It can be used in allergic conditions and in motion sickness. In the present study attempt has been made to formulate and optimize fast dissolving cinnarizine tablets containing different superdisintegrants viz cellactose 80, micro crystallian cellulose, tablettose 70 and spray dried lactose and to compare the optimized formulation of each superdisintegrant. The blend was examined for angle of repose, bulk density, tapped density and hausner's ratio. The tablets were evaluated for hardness, drug content, friability and disintegration time. It was concluded that the cellactose 80 has a great potential in the formulation of fast dissolving tablets of cinnarizine.
KEYWORDS: Fast dissolving tablets, Cinnarizine, Sodium starch glycolate, Superdisintegrants.

INTRODUCTION

The concept of Fast dissolving drug delivery system emerged from the desire to provide patient with conventional means of taking their medication[1]. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and paediatrics, because of physiological changes associated with these groups of patients[2]. Solid dosage forms that can be disintegrated, dissolved or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the pediatric and geriatric population, as well as other patients who prefer the convenience of easily swallowable dosage forms[3]. The tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva[4]. FDDS allow the luxury of much more accurate dosing than the primary alternative, oral liquids. Fast dissolving tablets are gaining prominence as new drug delivery systems[5].

Cinnarizine is chemically 1-benzhydryl 1-4-cinnamyl piperazine. It acts as histamine H1 antagonist and calcium channel blocker. It binds to histamine H1 receptor and to muscarinic acetylcholine receptors. Cinnarizine also inhibits contractions of vascular smooth muscle cells by blocking calcium channels. It is used for treatment of vertigo / menieres disease, nausea, vomiting, motion sickness and also useful for vestibular symptoms of other origins[6, 7]

In the present study attempt has been made to formulate fast dissolving tablets using different superdisintegrants cellactose 80, tablettose 70, micro crystalline cellulose and spray dried lactose[8, 9].

MATERIALS AND MEHODS

Cinnarizine was a gift from Rakshit pharma, Mumbai. Cellactose 80 and Tablettose 70 were gifted from Meggle pharma, Germany. MCC and Spray dried lactose were gifted from Maple Biotech Pvt Ltd, Pune.

PREFORMULATION STUDIES[10, 11]:

The granules are evaluated for angle of repose, bulk density, tapped density, carr's index and hausner's ratio.

PREPARATION OF CINNARIZINE FAST DISSOLVING TABLETS BY DIRECT COMPRESSION METHOD[12, 13]:

Drug, superdisintegrant, directly compressible material, diluents were passed through sieve #60. All the above ingredients were co-ground and properly mixed using mortor pestle for 5 mins. Talc and magnesium stearate were passed through sieve #80, mixed and blended with initial mixture. The powder blend was compressed into tablets using 8 mm normal concave punches to get tablets of 200 mg weight on a 12-station rotary tablet machine (Rimek Mini Press-1). Ingredients are depicted in Table 1.

WEIGHT VARIATION TEST:

Weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weight to the average.

FRIABILITY:

Friability is performed to assess the effect of friction. Roche Friabilator was used for the purpose.

DISINTEGRATION TIME[15]:

The test was carried out on 6 tablets using apparatus specified in I.P 1996 distilled water at $37^0C \pm 2^0C$ was used as disintegration media and time taken for complete disintegration was measured in seconds.

WETTING TIME[16]:

The method reported by yunixia et.al was followed to measure the table wetting time. A piece of tissue paper folded twice was placed in a small petridish containing 6ml of PH6.8. A tablet was put on the paper and the time for complete wetting was measured.

EVALUATION OF FORMULATED TABLET

TABLET HARDNESS[14]:

The strength of tablet is expressed as tensile strength kg/cm^2. The tablet crushing load, which is the force required to break a tablet by compression. It was measured using a tablet hardness tester (Pfizer Hardness Tester).

INVITRO DRUG RELEASE OF FORMULATED TABLETS:

The dissolution of cinnarizine tablets was carried out in basket type dissolution apparatus. The dissolution medium was 900 ml of gastric simulated fluid pH 1.2 maintained at 37 C. The basket was rotated at 50 rpm for 20 min. The sample was withdrawn after every 5 min and its absorbance was measured at 254 nm.

Data revealed in Table 2.

Table 1: Formulation of Batches N1 to N12

Batch	N1	N2	N3	N4	N5	N6	N7	N8	N9	N10	N11	N12
Drug(mg)	25	25	25	25	25	25	25	25	25	25	25	25
SSG(%w/w)	4	4	4	4	4	4	4	4	4	4	4	4
Cellactose (%w/w)	20	30	50	-	-	-	-	-	-	-	-	-
MCC(%w/w)	-	-	-	20	30	50	-	-	-	-	-	-
Tablettose (%w/w)	-	-	-	-	-	-	20	30	50	-	-	-
Spray dried lactose(w/w)	-	-	-	-	-	-	-	-	-	20	30	50
Mg. Stearate(w/w)	1	1	1	1	1	1	1	1	1	1	1	1
Talc(w/w)	2	2	2	2	2	2	2	2	2	2	2	2
Lactose	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total wt. (mg)	200	200	200	200	200	200	200	200	200	200	200	200

Table 2: Evaiuation of Batches N1 to N12

Batch	Disintegration time (sec)	Wetting time (sec)	Hardness Kg/cm^2	Friability (%) (n=10)	Drug release Q_{15}
N1	15 ± 2	33 ± 1.58	2 ± 0.5	1.45 ± 0.11	95.51 ± 0.61
N2	30 ± 3	45 ± 2.60	3 ± 0.3	0.91 ± 0.12	93.17 ± 0.35
N3	31 ± 3.60	35 ± 2.35	4 ± 0.55	0.55 + 0.06	92.17 ± 0.93
N4	25 ± 2.63	35 ± 1.60	3 ± 0.5	0.65 + 0.06	93.05 ± 0.22
N5	40 ± 2.6	40 ± 3.46	4.5 ± 1.32	0.42 ± 0.03	86.09 ± 2.05
N6	60 ± 4.48	70 ± 4.35	5 ± 0.86	0.34 ± 0.01	75.51 ± 0.51
N7	25 ± 3.60	25 ± 3.60	2.5 ± 0.55	1.35 ± 0.06	90.64 ± 1.20
N8	35 ± 2.65	45 ± 3.90	3 ± 0.5	0.76 ± 0.04	88.11 ± 0.78
N9	40 ± 1.7	45 ± 4.5	5 ± 0.43	0.51 ± 0.03	82.53 ± 1.40
N10	18 ± 2.64	30 ± 1	2 ± 0.36	0.94 ± 0.02	86.61 ± 0.42
N11	40 ± 3.60	65 ± 1.73	3.5 ± 0.88	0.56 ± 0.04	85.5 ± 0.84
N12	40 ± 3	70 ± 4.20	4.5 ± 0.9	0.34 ± 0.04	70.61 ± 0.61

OPTIMIZATION OF FORMULA:

From different formulations four batches viz. N_3, N_4, N_8 and N_{11} were selected considering all parameters of fast dissolving tablets.

STABILITY STUDIES[17, 18]:

The stability studies of optimized formulations was carried out at different conditions for 30 days. The effects of temperature and time on physical characteristics of the tablet were evaluated for assessing the stability of prepared formulations. The different parameters that were studied are hardness, disintegration time, friability and dissolution rate.

Data revealed in Table 3 & 4.

Table 3: Stability studies data for optimized batches

Batch No.	Parameters	Initial	After 30 days		
			25^0C, 60% RH	30^0C, 65% RH	40^0C, 75%, RH
N3	Disintegration time	31	31	30	28
	Hardness	4	4	3.8	3.7
	Friability	0.55	0.57	0.59	0.62
	Assay %	100.3	99.92	99.81	99.67
N4	Disintegration time	24	24	22	21
	Hardness	3	3	2.8	2.6
	Friability	0.65	0.67	0.74	0.74
	Assay%	99.48	99.32	98.48	98.84
N8	Disintegration time	35	33	32	30
	Hardness	3	2.9	2.8	2.6
	Friability	0.76	0.78	0.79	0.82
	Assay%	99.12	99.01	98.70	98.12
N11	Disintegration time	40	38	35	32
	Hardness	3.5	3.5	3.4	3.2
	Friability	0.56	0.56	0.61	0.65
	Assay%	99.35	99.35	98.87	98.49

Table 4: Dissolution Data for drug release from batches kept at different conditions. (After 30 days)

	Time(min)	$25^0C + 2^0C$ RH 60% + 5%	$30^0C + 2^0C$ RH 65% + 5%	$40^0C + 2\%$ RH 75% + 5%
N3	1	44.71	42.80	41.25
	2	75.68	73.56	72.87
	3	93.20	92.81	92.20
	4	99.60	99.34	99.13
	5	100.20	99.91	99.78
N4	1	47.21	46.40	45.18
	2	76.19	74.89	74.33
	3	87.34	88.11	87.69
	4	98.21	97.94	97.78
	5	99.70	99.25	98.81
N8	1	41.25	40.50	40.08
	2	72.87	71.24	71.18
	3	92.24	90.89	87.92
	4	98.07	97.12	94.89
	5	98.84	98.42	98.11
N11	1	37.88	36.57	36.40
	2	68.91	65.79	64.22
	3	87.25	86.11	85.89
	4	96.83	96.40	95.78
	5	98.90	98.73	98.03

RESULTS AND DISCUSSION

The use of superdisintegrants for preparation of fast dissolving tablets is highly effective and commercially feasible. These superdisintegrats accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking tablets and therefore disintegration. The disintegration is reported to have an effect on dissolution characteristics as well.

Fast dissolving cinnarizine tablets were prepared using different superdisintegrants. Twelve batches of tablets were prepared by varying the concentrations of superdisintegrants. Tablets were prepared by direct compression method. Tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variation as per pharmacopoeial specifications. The hardness and friability were within limits indicating good mechanical resistance (Values revealed in Table 2).

Considering all the formulations of N_1 to N_{12} batches, In preliminary study N_3 formulation having 50% cellactose gave best results of hardness of 4 kg/cm^2, friability of 0.55, disintegration time of 31 sec and wetting time of 35 sec. N_4 formulation having 20% MCC gave best results of hardness of 3 kg/cm^2, friability of 0.63, disintegration time of 25 sec and wetting time of 35 sec. while N_8 having 30% tablettose gave best results of hardness of 3kg/cm^2, friability of 0.76, disintegration time of 35 sec and wetting time of 45 sec. N_{11} formulation having 30% spray dried lactose gave best results of hardness of 5kg/cm^2, friability of 0.56, disintegration time of 40 sec and wetting time of 65 sec. But considering all parameters of fast dissolving tablets it can be concluded that 50% cellactose gave good results so it can be used as diretly compressible materials.

Stability studies of formulations N_3, N_4, N_8 and N_{11} was carried out at different conditions for 30 days. The tablets are evaluated for hardness, friability, disintegration time, assay and In-vitro drug release (Values revealed in Table 3 & 4). The results of stability studies showed the physical and chemical properties of the tested tablets were not altered significantly in all four formulations. So these may be considered as stable formulations. The formulation N_3 showed lesser fluctuations in all evaluation parameters than other formulations. So formulation N_3 containing 50% cellactose is the most stable among all formulations.

CONCLUSION

In the present study it was concluded that cinnarizine fast dissolving tablets are prepared successfully by using different superdisintegrants viz. Cellactose 80, tablettose 70, MCC and spray dried lactose. Overall study suggests that the cellactose 80 has a great potential in the formulation of fast dissolving tablets of cinnarizine.

Figure No.1 Release profile of preliminary trial of cellactose

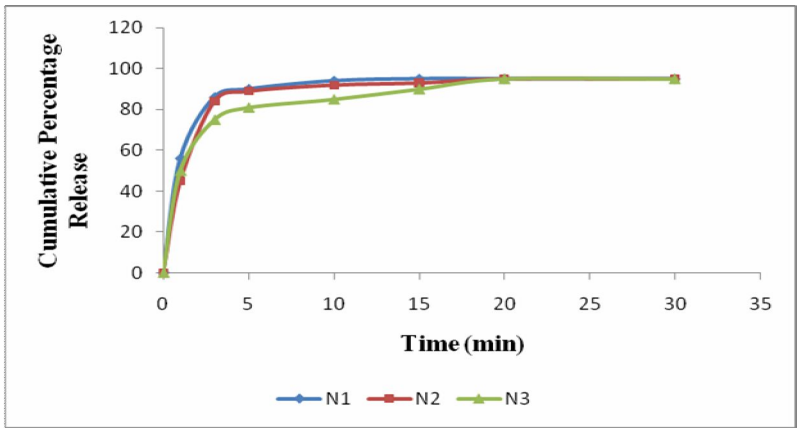


Figure No.2 Release profile of preliminary trial of MCC

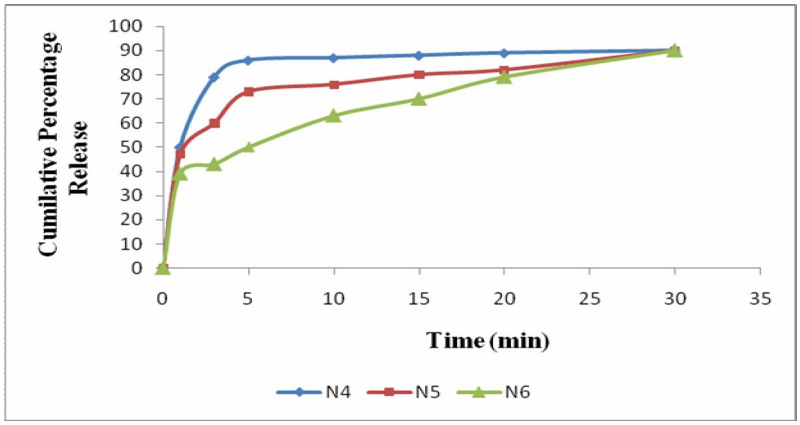


Figure No. 3 Release profile of preliminary trial of tablettose

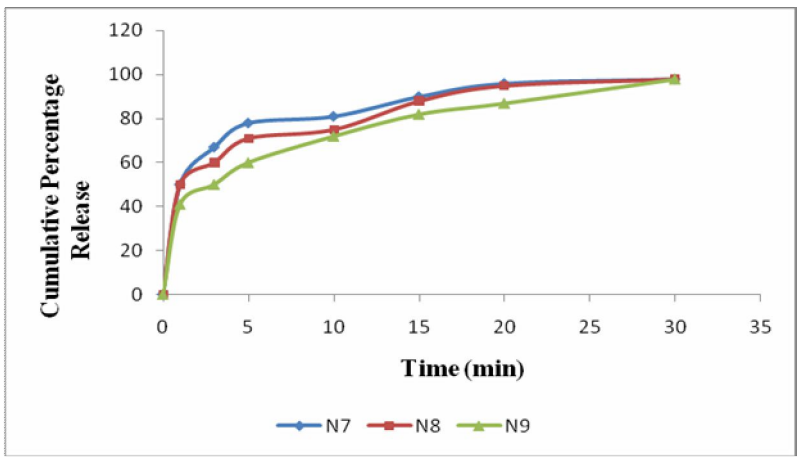
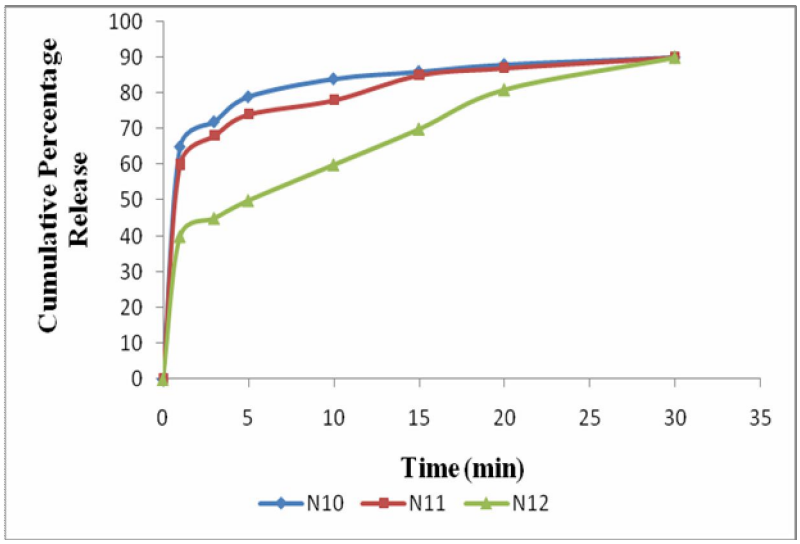


Figure No. 4 Release profile of preliminary trial of spray dried lactose



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