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RESEARCH ARTICLE

FORMULATION AND EVALUATION ORAL DISPERSIBLE TABLET OF CINNARIZINE

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ABSTRACT

Oral Dispersible tablets (ODTs) constitute an innovative dosage form, which overcomes the problem of swallowing and provides a quick onset of action. The aim of the proposed work is to formulate fast dissolving tablets of Cinnarizine for rapid dissolution of drug and absorption, which may produce rapid onset of action in the treatment of motion sickness. For this purpose the tablets of Cinnarizine were prepared by Effervescent method, Super disintegrants addition method and Sublimation method. Cinnarizine is an Antihistamines drug has been used for the treatment of motion sickness. Cinnarizine is poorly soluble in water making it a potent candidate fast-dissolving drug delivery system.

Key word: ODT, Cinnarizine, Granules, Superdisintegrants,

INTRODUCTION

Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is Fast Dissolving Tablet (ODT). [1-4]

The term ODT appears in the European Pharmacopoeia defined as ''uncovered tablet for buccal cavity, where it disperses before ingestion". The solid ODT dosage form turns into a soft paste or liquid form for easy swallowing, and thus it is free of suffocation risk. ODTs are beneficial for paediatric, geriatric, schizophrenic, bedridden patients and those with Parkinsonism or developmentally disabled patients with persistent nausea and patients who have little or no access to water. ODT will avoid missing out of dose even during travelling, busy or other situations where there is no access to water. They undergo disaggregation in the mouth when in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. A major claim of some oral dispersible tablets is increased bioavailability compared to traditional tablets because some of the drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, the bioavailability of the drug is significantly increased over those observed in the conventional tablet dosage form. [5-8]

MATERIALS AND METHODS

Sublimation method

Specified quantity of Cinnarizine, camphor, mannitol, aspartame, talc and magnesium stearate were weighed accurately and were passed through 60 # screen prior to mixing. All the materials were transferred to mortar and triturated till it mixed uniformly. The resulting powder mixture was compressed into tablets using single punch tablet machine. The tablets were dried at 60^{o}C oven till constant weigh obtained. [9-10]

EVALUATION OF POWDER BLEND

Table 1: Evaluation of the Powder Blend

Batch code	Bulk density	Tapped density	Angle of repose	% compressibility	Hausner ratio
B1	0.58	0.68	25.61	14.71	1.172
B2	0.56	0.67	25.07	16.42	1.196
B3	0.55	0.64	24.68	14.06	1.164
B4	0.53	0.62	24.50	14.52	1.170
B5	0.52	0.59	23.82	11.86	1.135
B6	0.50	0.57	23.49	12.28	1.140
B7	0.58	0.70	30.05	17.14	1.207
B8	0.58	0.71	30.64	18.31	1.224
B9	0.59	0.73	31.45	19.18	1.237

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Formulation of Oral Dispersible Tablet

Table 2: Formulation of ODT

Ingredient	B1	B2	B3	B4	B5	B6	B7	B8	B9
Cinnarizine	25	25	25	25	25	25	25	25	25
Crospovidone	10	15	20		-	-	-	-	-
Croscarmellose sodium	-	-	-	10	15	20	-	-	-
L-HPC	-	-	-	-	-	-	10	15	20
Avicel 102	60	60	60	60	60	60	60	60	60
Aspartame	2	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4	4
Mg stearate	2	2	2	2	2	2	2	2	2
Mannitol up to…	200	200	200	200	200	200	200	200	200

EVALUATION OF ORAL DISPERSIBLE TABLETS

Table 3: physical parameters of mouth dissolving Tablet

Batch Code	Weight Variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	In-Vitro Disin. Time (Sec)	Wetting Time (Sec)	Assay (%)
B1	pass	2.56	2.5	0.73	48.3 ±1.53	69.8 ±1.04	98.14
B2	pass	2.57	2.5	0.76	34.0 ±1.00	35.0 ±0.95	99.02
B3	pass	2.60	2.5	0.79	28.6 ±1.22	32.4 ±1.15	100.51
B4	pass	2.63	2.5	0.74	59.4 ±2.42	89.0 ±0.85	98.91
B5	pass	2.65	3.0	0.78	32.6 ±1.25	66.0 ±1.35	100.04
B6	pass	2.66	2.5	0.80	36.6 ±2.12	70.4 ±1.48	99.86
B7	pass	2.51	3.0	0.69	59.7 ±2.46	67.8 ±0.35	98.92
B8	pass	2.52	2.5	0.65	33.5 ±0.50	41.7 ±1.45	101.05
B9	pass	2.54	2.5	0.66	25.3 ±0.58	29.1 ±1.05	100.34

3. In-vitro Disintegration time

The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds. [11]

Table 4: Evaluation parameter of mouth dissolving tablets prepared by different method

Parameters	Effervescent	Superdisintegrant addition	Sublimation
Hardness (kg/cm^2)	2.5	2.5	2.5
Friability (%)	0.625	0.764	0.861
Disintegration time (s)	92	34	132

The disintegration time and friability were evaluated and results were graphically summarized in the Figure 1 and Figure 2

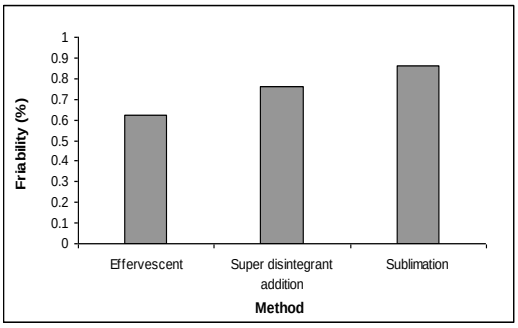

Figure 1: Column graph of friability of mouth dissolving tablets prepared by different method

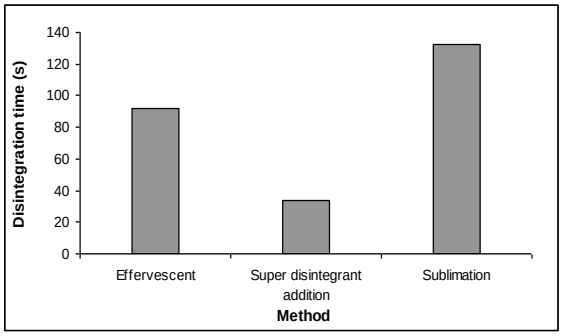

Figure 2: Column graph of disintegration time of mouth dissolving tablets prepared by different method

The friability of tablets, prepared by various methods was shown in Fig. No 1. Friability of all batches was in the range of standard limit (less than 1%) and no more significant difference. It can be concluded that tablets prepared by superdisintegrant addition method has less disintegration time than other method. [12-15]

STUDY OF THE EFFECT OF CONCENTRATION OF AVICEL PH 102

The intermediate concentration of the diluent (Avicel PH 102), that is, 20 - 50 % of the tablet weight was selected from the trial series. These trial batches were prepared by super disintegrant addition method with same process as above.[16-17]

Table 5: Composition of formulation of Trial series

Ingredient	T1	T2	T3	T4
Cinnarizine	25	25	25	25
Crospovidone	15	15	15	15
Avicel PH 102	40	60	80	100
Aspartame	2	2	2	2
Talc	4	4	4	4
Mg stearate	2	2	2	2
Mannitol up to…	200	200	200	200

All the quantities are in mg.

These tablets were evaluated for hardness, friability and disintegration time. The procedure was same as above evaluation tests.

Table 6: Evaluation parameter of Trial series

Parameter	T1	T2	T3	T4
Hardness (kg/cm^2)	2.5	2.5	2.5	2.5
Friability (%)	2.24	0.76	0.62	0.45
Disintegration time (s)	27	34	48	64

The friability and disintegration time were evaluated and results are graphically summarized in the Fig. No 3 and Fig. No 4.

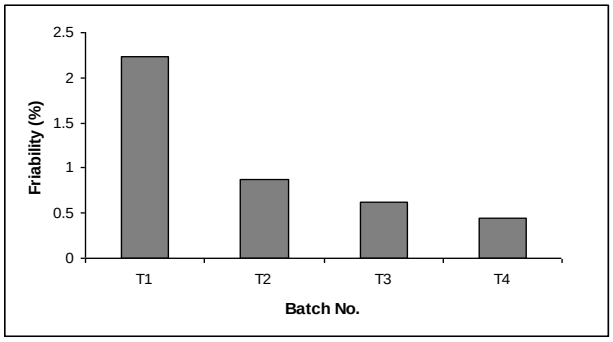

Figure 3: Column graph of the % Friability of trial series

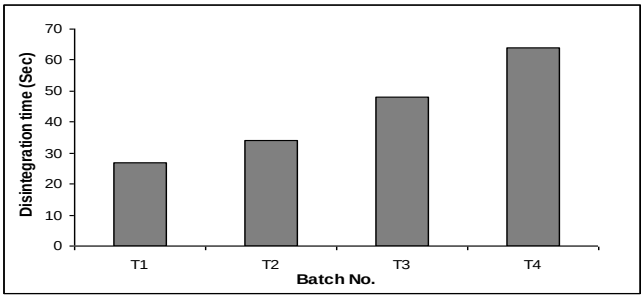

Figure 4: Column graph of the Disintegration time (Sec) of trial series

8. In-Vitro drug release:

Release of the drug *in vitro*, was determined by estimating the dissolution profile.

Dissolution test:

Standard USP or IP dissolution apparatus have been used to study in vitro release profile using rotating paddle.*In vitro* release rate study of mouth dissolving tablet of Cinnarizine was carried out using the Apparatus 2 (Paddle apparatus) method. The dissolution apparatus was covered with the black color polythine to protect the solution from light. The dissolution test was carried out using 900 ml of 0.1 N HCl, at 37 $\pm$ 0.5^{0}C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 2, 4, 6, 8 and 10 min and withdrawn volume was replaced with fresh dissolution media. [18-20]

The withdrawn samples diluted with dissolution medium and then filter it with whattman filter paper and assayed at 253.5 nm. The % release of Cinnarizine was calculated.

Table 6: Percentage Cumulative drug release profile of batch B1

Time (min)	Absorbance	Concentration (µg/ml)	Amt. in 5 ml (mg/ml)	Amt. in 900 ml (mg/ml)	Cumulative drug release in 900 ml (mg)	Cumulative % drug release
0	0	0	0	0	0	0
2	0.0764	1.46	0.0073	13.12	13.12	52.49
4	0.1178	2.25	0.0112	20.23	20.24	80.96
6	0.1387	2.65	0.0132	23.82	23.84	95.36
8	0.1422	2.71	0.0136	24.42	24.46	97.82
10	0.1425	2.72	0.0136	24.48	24.52	98.08

Table 7: Percentage Cumulative drug release profile of batch B2

Time (min)	Absorbance	Concentration (µg/ml)	Amt. in 5 ml (mg/ml)	Amt. in 900 ml (mg/ml)	Cumulative drug release in 900 ml (mg)	Cumulative % drug release
0	0	0	0	0	0	0
2	0.0968	1.85	0.0092	16.63	16.63	66.50
4	0.1262	2.41	0.0120	21.68	21.68	86.74
6	0.1416	2.70	0.0135	24.32	24.34	97.37
8	0.1438	2.74	0.0137	24.70	24.73	98.93
10	0.1439	2.75	0.0137	24.72	24.76	99.06

Table 8: Percentage Cumulative drug release profile of batch B3

Time (min)	Absorbance	Concentration (µg/ml)	Amt. in 5 ml (mg/ml)	Amt. in 900 ml (mg/ml)	Cumulative drug release in 900 ml (mg)	Cumulative % drug release
0	0	0	0	0	0	0
2	0.1021	1.95	0.0097	17.54	17.54	70.15
4	0.1294	2.47	0.0123	22.23	22.23	88.94
6	0.1452	2.77	0.0139	24.94	24.96	99.84
8	0.1459	2.78	0.0139	25.06	25.10	100.38
10	0.146	2.79	0.0139	25.08	25.13	100.50

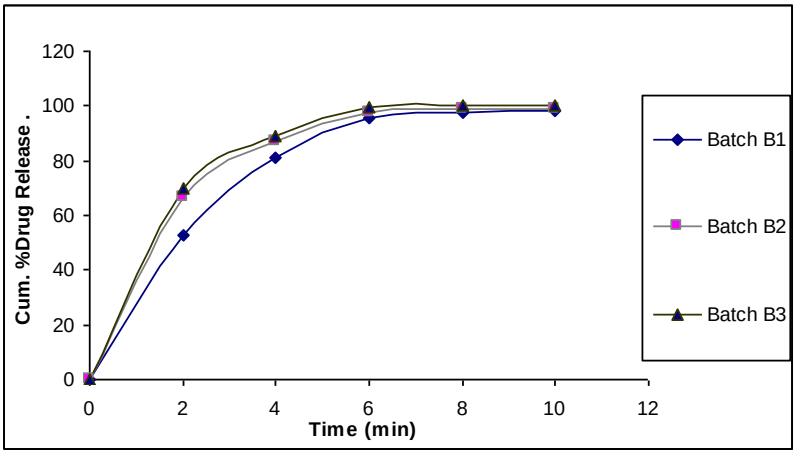

Figure 5: Cumulative drug release profile of batch B1, B2 and B3

Table 9: Percentage Cumulative drug release profile of batch B9

Time (min)	Absorbance	Concentration (µg/ml)	Amt. in 5 ml (mg/ml)	Amt. in 900 ml (mg/ml)	Cumulative drug release in 900 ml (mg)	Cumulative % drug release
0	0	0	0	0	0	0
2	0.1211	2.31	0.0116	20.80	20.80	83.20
4	0.1397	2.67	0.0133	23.99	24.01	96.02
6	0.1452	2.77	0.0139	24.94	24.96	99.86
8	0.1456	2.78	0.0139	25.01	25.05	100.19
10	0.1455	2.78	0.0139	24.99	25.04	100.17

COMPARISON OF BEST FORMULATED TABLET WITH MARKETED TABLET

The best formulated tablet was then compared with marketed tablet STUGERON 25mg. Formulation B9 was compared with marketed tablet for *in vitro* dissolution study.

Table 10: Percentage Cumulative drug release profile of Marketed Tablet

Time (min)	Absorbance	Concentration (µg/ml)	Amt. in 5 ml (mg/ml)	Amt. in 900 ml (mg/ml)	Cumulative drug release in 900ml (mg)	Cumulative % drug release
0	0	0	0	0	0	0
2	0.0326	0.62	0.0031	5.60	5.60	22.40
4	0.0365	0.70	0.0035	6.27	6.27	25.09
6	0.0462	0.88	0.0044	7.94	7.94	31.77
8	0.0602	1.15	0.0057	10.34	10.35	41.40
10	0.0731	1.40	0.0070	12.56	12.57	50.29
15	0.0993	1.90	0.0095	17.06	17.08	68.32
30	0.1307	2.49	0.0125	22.45	22.48	89.93
45	0.1453	2.77	0.0139	24.96	25.00	100.01

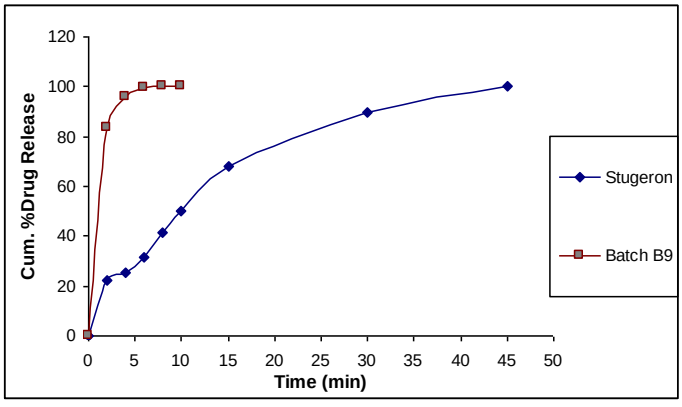

Figure 6: Comparison of in-vitro dissolution of B9 with marketed tablet

SUMMARY AND CONCLUSION

The present study was undertaken with an aim to formulate and evaluate Fast Dissolving tablets of Cinnarizine using Sublimation method with the addition of superdisintegranting agents. To increase the dissolution rate of poorly soluble drug Cinnarizine, by using the addition of Avicel 102 as Superdisintegrants. Preformulation study was carried out initially and results directed for the further course of formulation. Various formulations of Fast Dissolving tablets Cinnarizine were formulated by using various super Disintegrants—

Crosspovidone, Sodium Starch Glycolate, Crosscarmellose Sodium. The tablets were evaluated for physical parameter such as Hardness, thickness, weight variation, friability, in-vitro disintegration, wetting time and In-Vitro Dissolution. Disintegration time of optimized formulation B9 was compared to conventional tablets, where it observed that disintegration time less than market preparation.

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