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FORMULATION, DEVELOPMENT AND CHARACTERIZATION OF ORAL DISINTEGRAING TABLET OF CIMITIDINE HCL

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ABSTRACT

Cimitidine HCl is a recognized drug for peptic ulcer therefore development of an ODT of Cimitidine HCl and to evaluate the effect of various superdisintegrants on its disintegration time and release profile was the prime objective of this research work. Tablets were prepared by direct compression technique using 3 different superdisintegrants. Sodium starch glycolate, Croscarmellose sodium and Crosspovidone XL-10 were used as superdisintegrants in combinations and individually to achieve optimum release profile, disintegration time and hardness. Direct compression process was selected for this formulation of ODT tablets, because porous nature is more in direct compression blend than wet granulation blend, so it will give faster disintegration. Microcrystalline cellulose was used as diluent and mannitol, mint flavor and sodium saccharin were used to enhance the organoleptic properties of tablets. The tablets were evaluated for weight variation, hardness, friability, in-vitro disintegration time and drug release characteristics. Hardness and friability data indicated good mechanical strength around 3 kg/cm2 for all the batches. The results of in-vitro disintegration time indicated that the tablets dispersed rapidly in mouth within 30s. It was concluded that superdisintegrants addition technique is a useful method for preparing orally disintegrating tablets by direct compression method.

KEYWORDS: Cimitidine HCl.

INTRODUCTION

Orally Disintegrating Tablet

Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. The important drawback of tablets and capsules dosage forms for pediatric and geriatric patients is being difficulty in swallowing.

To overcome these problems, formulators have considerably dedicated their effort to develop novel drug delivery systems (NDDS) which enhance safety and efficacy of drug molecule and to achieve better patient compliance. One such approach is 'Oral dispersible Tablets', which disintegrate or dissolve in saliva and are swallowed without water as tablet disintegrate in mouth, this could enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx, esophagus. This leads to an increase in the bioavailability by avoiding first pass liver metabolism.[1,2]

MATERIALS AND METHODS

Materials

Drug Cimitidine HCl(Unique Chemicals, Panoli, India), Indion 204(Degussa India Pvt. Ltd., Mumbai, India), Microcrystalline cellulose(Merk chemicals, Mumbai, India), Sodium Starch Glycollate(Meggle, Germany), Crospovidone(Colorcon Asia Pvt. Ltd. Goa, India), Croscarmellose Sodium(Loba chemicals , Mumbai, India), Aspartame(S.D.Fine Chemicals Ltd., Mumbai, India), Colloidal Silicon Dioxide (Aerosil 200)(Fine chemicals, Mumbai, India), Magnesium Stearate(Meggle, Germany), Chocolate(Loba chemicals , Mumbai, India), Pepper mint(Loba chemicals , Mumbai, India).

Method

Direct compression technique was used to prepare the tablets. Weigh and sift the dry complex, Mannitol, through 24 sieve. Disintegrates (Sodium Starch Glycollate, Croscarmellose Sodium, Crospovidone, Crospovidone XL 10) and ColloidalSilicon Dioxide through 30# sieve and Sweetner, Flavors, Lubricant through 60# sieve. Mix all the ingredients for 5 min. Lubricated powder were compressed into tablets using

12.0mm FFBE (Flat Face Bevel Edge) punch set using a twelve station tablet press. Compression was carried out using "D" tooling punches sets.

Table 1: Composition of Orally Disintegrating Tablet.

Sr. No.	Ingredients	Optimized batch (F18) (mg/tab)
1.	Drug Resin Complex (eq. to 200 mg Cimitidine HCl)	580
2.	Sodium Starch Glycollate	-
3.	Cross Carmellose Sodium	-
4.	Crospovidone	58
5.	Colloidal Silicon Dioxide	6
6.	Magnesium Stearate	3
7.	Mannitol	30
8.	Aspartame	10
9.	Chocolate Flavor	13
	Net Total	**700**

Evaluation of tablets

A) Physical Characterization

- **Physical appearance**

The general appearance and elegance of tablet was identified visually, which include tablet size, shape, color, presence or absence of an odor, taste, surface texture and avoid of sticking etc.

- **Hardness**

Tablets require certain amount of strength or hardness, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (crushing strength) is the Schleuniger hardness tester.

Method: Ten tablets were randomly selected and hardness was measured in Schleuniger hardness tester. The average was taken as hardness of the tablet.

- ***In vitro* disintegration test**

In vitro disintegration time was measured using USP disintegration test apparatus. Randomly six tablets were selected from each batch for disintegration test. Disintegration test was performed in 900ml distilled water at 37±0.5 °C temperature and at the rate of 30±2 cycles/min.

- **Thickness**

Ten Tablets were selected randomly from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement.

- **Friability**

Friability is related to the ability of tablet to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus (The Roche friabilator). Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered acceptable.

Method: Ten tablets were weighed (initial wt.) and then transfer into Rocha friabilator. It was subjected to 100 revolutions in 4 minutes. The tablets were dedusted and reweighed (final wt). These two weights were applied to following formula and friability was calculate

$$\% \text{ Friability} = \frac{(\text{Initial Weight} - \text{final weight})}{(\text{Initial weight})} \times 100$$

- **Wetting time**

For measurement of wetting time five circular tissue papers of 10 cm diameter are placed in a petri dish with a 10 cm diameter. 10 ml of water-containing Eosin, a water-soluble dye, is added to petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

- **Weight variation**

Twenty tablets were taken randomly, weigh individually and average weight was determined. The individual tablet weight was compared with average tablet weight.[6]

Table 2: Weight variation of tablets as per USP.

Avg. Weight(mg)	Maximum % difference allowed
130 or less	10
130-324	7.5
More than 324	5

Standard solution: Transfer an accurately weighed quantity of about 150 mg of Cimitidine HCl working standard to a 100-ml volumetric flask. Add about 50 ml of water and sonicate to In the present work stability study was carried out for the optimized formulation for following condition and time period, 40°C/ 75% RH for 6 months.[9] Development trials: Tablets were compressed at average wt. of 650±5.0 mg with thickness of 3.14±0.5 mm.

Table 3: ICH guide lines for stability study.

Study	Storage condition	Time period
Long term*	25°c±2°C/60% RH±5%RH or 30°c±2°C/65%RH±5 % RH	12 month
Intermediate**	30°c±2°c/65% RH±5% RH	6 month
Accelerated	40°c±2°c/75% RH±5% RH	6 month

Table 4: Physical Parameter of batch F1 to F18.

Batch	Hardness (kg/cm2)	Disintegrating time (sec)	Wetting time (sec)	Friability (%)
F1	3-4	83	83	0.34
F2	3-4	72	76	0.35
F3	3-4	63	63	0.19
F4	3-4	59	59	0.16
F5	3-4	56	57	0.14
F6	3-4	55	54	0.18
F7	3-4	53	50	0.15
F8	3-4	50	48	0.15
F9	3-4	46	49	0.18
F10	3-4	40	46	0.23
F11	3-4	37	47	0.19
F12	3-4	33	43	0.14
F13	3-4	29	39	0.09
F14	3-4	47	53	0.11
F15	3-4	51	59	0.21
F16	3-4	43	51	0.15
F17	3-4	34	45	0.14
F18	3-4	30	40	0.10

Table 5: Comparative dissolution study of Batch F1 to F6.

Time	F1	F2	F3	F4	F5	F6
0	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
5	30.1 ± 2.18	34.7 ± 1.58	37.5 ± 2.22	39 ± 1.00	40 ± 2.72	42.6 ± 3.00
10	51.4 ± 3.00	56.1 ± 2.10	59.3 ± 3.56	60 ± 1.76	61 ± 3.35	62.7 ± 1.00
15	63.1 ± 2.58	68.4 ± 4.18	70 ± 4.10	71.5 ± 2.90	72.7 ± 1.20	73.2 ± 4.00
20	72.8 ± 1.51	76 ± 2.80	81 ± 2.00	82.3 ± 3.00	83.6 ± 3.40	84.5 ± 2.26
30	85.9 ± 3.10	88.1 ± 3.25	90.2 ± 1.10	91 ± 2.15	92 ± 2.86	93.2 ± 1.34

n = 6

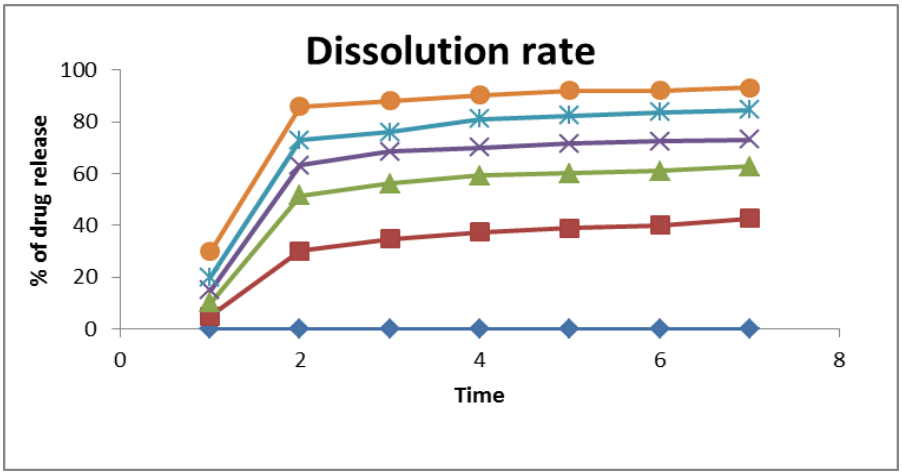


Figure 1: Comparative dissolution profile of batch F1,F2 and F6.

Table 6: Comparative dissolution study of Batch F7 to F12.

Time	F7	F8	F9	F10	F11	F12
0	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
5	44.1 ± 2.30	46.3 ± 1.49	48.9 ± 2.30	52 ± 4.43	54.7 ± 1.18	58.9 ± 2.76
10	63.9 ± 3.15	65.1 ± 2.50	67.4 ± 2.50	69.2 ± 3.80	71.1 ± 2.17	73.2 ± 2.87
15	74.5 ± 2.98	75.2 ± 3.60	76.9 ± 1.80	77.1 ± 2.16	79.4 ± 3.16	80.6 ± 3.00
20	85.4 ± 3.00	86.1 ± 1.50	87.7 ± 3.42	88 ± 1.80	89.2 ± 2.14	90 ± 1.60
30	94.5 ± 1.34	95.9 ± 3.98	96.7 ± 2.00	97.3 ± 2.00	98.9 ± 1.00	99.7 ± 1.30

n = 6

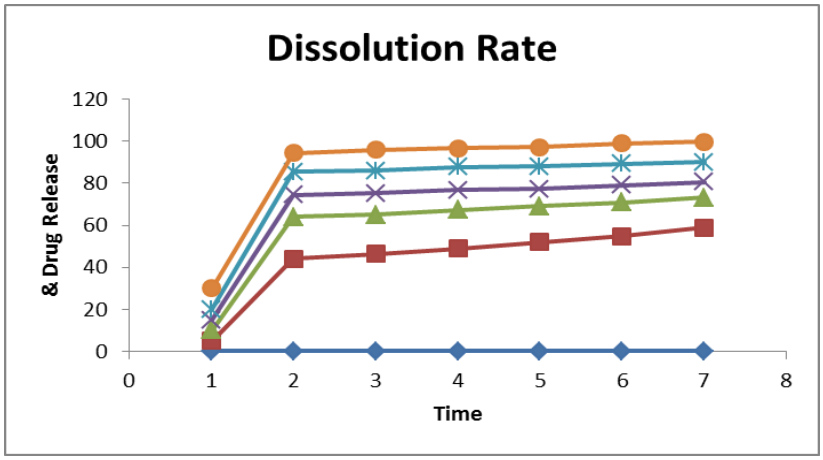
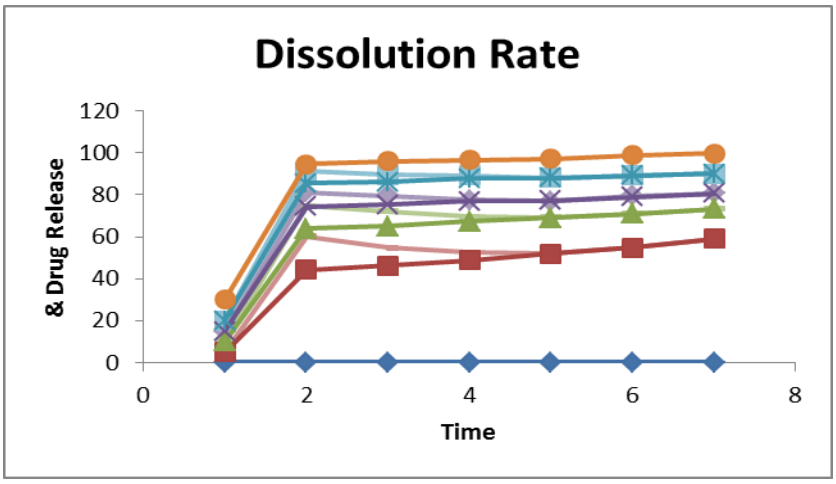


Figure 1: Comparative dissolution profile of batch F7,F8 and F12.

Table 6: Comparative dissolution study of Batch F13 to F18.

	F13	F14	F15	F16	F17	F18
0	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
5	60.1 ± 2.34	54.8 ± 3.76	52.5 ± 3.23	52 ± 4.43	54.7 ± 1.18	58.9 ± 2.76
10	74.9 ± 3.00	72.1 ± 2.10	69.7 ± 1.78	69.2 ± 3.80	71.1 ± 2.17	73.2 ± 2.87
15	81.2 ± 1.90	79.4 ± 3.45	77.6 ± 2.56	77.1 ± 2.16	79.4 ± 3.16	80.6 ± 3.00
20	91.2 ± 2.60	89.6 ± 2.45	89.1 ± 2.18	88 ± 1.80	89.2 ± 2.14	90 ± 1.60
30	99.7 ± 2.56	98.1 ± 3.00	97.5 ± 1.96	97.3 ± 2.00	98.9 ± 1.00	99.7 ± 1.30

n = 6



CONCLUSION

In present research oral dispersible tablet of Cimitidine HClwas prepared with the aim of taste masking and low disintegration time. Complex was prepared using resin Indion 214, Kyron T-114, Indion 204. Indion 204 showed best result and was selected for tablet formulation. Different super disintegrants like sodium starch glycollate, cross carmellose sodium and crospovidone were used alone and in combination. Crospovidone 58 mg showed desired result and was

selected for optimization and stability analysis. A successful ODT was formulated with 1:2 Drug: Resin ratio and 58mg of crospovidone which showed disintegration time of 30 seconds.

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