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Der Pharmacia Lettre, 2010, 2(3): 342-351
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Preparation and Evaluation of Fast Disintegrating Tablets of Dicyclomine HCl

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Abstract

The purpose of the present research is to prepare Fast Disintegrating Tablets of Dicyclomine Hydrochloride and evaluate the effect of super-disintegrants on disintegration behavior. Fast Disintegrating tablets of Dicyclomine Hydrochloride were prepared using sodium starch glycolate together with Micro crystalline cellulose as superdisintegrants. Mannitol was used as diluents and saccharin sodium was used as sweetener for taste masking. All the formulations showed weight variation less then 103.89 ±0.41 with in-vitro disintegration time less than 40 seconds. The results revealed that the tablets bear a good dissolution profile. The drug content of all the formulations was within the acceptable limits of the United States Pharmacopoeia XXVII. This work will help in understanding the effect of superdisintegrants on disintegration behaviour of tablet, dissolution, absorption and finally the bioavailability of drug. The present study demonstrated potentials for rapid disintegration/dissolution, absorption, improved bioavailability, effective therapy and improved patient compliance.

Keywords: Mouth Disintegrating tablet, Dicyclomine HCl, Superdisintegrant, Direct compression.

INTRODUCTION

Swallowing a pill is a major difficulty encountered in case of geriatric and pediatric patient which leads to poor patient compliance due to unpalatable taste of drug. To troubleshoot this problem a new dosage form known as fast-dissolving/disintegrating tablet (FDT), has been developed which rapidly disintegrate and dissolve in saliva. FDT are intended and designed to disintegrate and dissolve in saliva and then easily swallowed without need of water which is a

major benefit over conventional dosage form. These dosage forms are also used to attain instant a higher concentration of drug in body for immediate actions.[1,2] Mouth dissolving/disintegrating tablets combine the advantage of both liquid and conventional tablet formulations allowing the ease of swallowing the drug in the form of liquid dosage form. Some 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. The basic approach for the development of mouth Disintegrating tablets is the use of superdisintegrants to produce micro maximizing the pore structure of the tablet matrix,[3] freeze drying and vacuum drying techniques have been tried by researchers to maximize the pore structure of the tablet matrix. However, freeze drying is cumbersome and yields a fragile and hygroscopic product.[4] Vacuum drying along with the sublimation of volatilizable ingredient has been employed to increase tablet porosity. While designing dispersible tablets, it is possible to achieve effective taste masking as well as a pleasant feel in the mouth. The main criterion for fast disintegrating tablets is the ability to disintegrate or dissolve rapidly in saliva of the oral cavity in 15 to 60 seconds and have a pleasant mouth feel.
Dicyclomine Hydrochloride is a anti-spasmodic drug. In the present study, an attempt was made to develop mouth disintegrating tablets of Dicyclomine HCl and to investigate the effect of superdisintegrants on the release profile of the drug in the tablets.[5]

MATERIALS AND METHODS

Materials

Dicyclomine HCl was obtained as a gift from Bavaria Pharma Vadodara, Mumbai. sodium starch glycol late (SSG) and Micro crystalline cellulose(MCC) were also gifts from Vijalak Pharma LTD., Hydrabad, Andhra Pradesh, India, sodium saccharin, mannitol, polyvinyl pyrollidone(PVP), talc and magnesium stearate were purchased from Central Drug House (P) LTD. New Delhi. S.D. Fine Chemicals, Mumbai, India.Menthol were purchase from Bhagat Aromatics Limited, India.

Method

Formulation of mouth Disintegrating tablets

The fast Disintegrating tablets of Dicyclomine HCl were prepared using the SSG and microcrystalline cellulose as superdisintegrants, mannitol as a diluent, sodium saccharin as sweetening agent, PVP as binder and magnesium stearate as a glidnat (Table 1). The drug and other ingredients were mixed together in mortal and pestle for 15 min. Direct compression method was used to prepare tablets. In formulation of tablets using a 4mm punch rotary tablet machine (Rimek, RSB-4 mini press Cadmach,Ahmedabad, India).[4,5]

Table 1: Composition of different batches of Fast-Disintegrating tablets of Dicyclomine HCl.

Ingredient	F1(mg)	F2(mg)	F3(mg)	F4(mg)	F5(mg)	F6(mg)	F7(mg	F8(mg))	F9(mg)
Dicyclomine HCl	20	20	20	20	20	20	20	20	20
Mannitol	41	41	41	41	41	41	41	41	41
Sodium starch glycolate	10	6.66	5	4	3.33	16.67	16	15	13.67
Micro crystalline cellulose	10	13.67	15	16	16.67	3.33	4	5	6.66
PVP	15	15	15	15	15	15	15	15	15
Mg-stearate	2	2	2	2	2	2	2	2	2
Menthol	1	1	1	1	1	1	1	1	1
Na-sachrine	1	1	1	1	1	1	1	1	1

Table 2: Bulk Characterization of Blend

Bulk characterization	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density gm/cm3	0.33	0.28	0.31	0.34	0.32	0.33	0.31	0.33	0.33
Tapped densitygm/cm3	0.5	0.5	0.48	0.51	0.48	0.5	0.47	0.51	0.5
Porosity (%)	66	66	65	65	65	66	66	65	66
Carrs index(%)	34	44	35.4	33	34	34	34	34	34
Hausner index(%)	1.5	1.7	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Angel of repose(^{0})	19.4	15.16	15.49	16.08	16.20	97.24	17.41	15.31	14.80

Evaluation of Blend [6]

Firstly compression into tablets, the blend were evaluated for following pre compression properties which includes parameters.

1. Angle of repose

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, h, was obtained. Diameter of heap, D, was measured. The angle of repose, Θ, was calculated by formula

$$\tan \Theta = h / r$$

$$\Theta = \tan^{-1} (h / r)$$

Where, Θ is the angle of repose, h is the height in cm and r is the radius.

2. Bulk Density

Apparent bulk density was determined by pouring pre- sieved drug excipient blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/ml and is given by

$$D_b = M / V_0$$

Where, M is the mass of powder and V0 is the Bulk volume of the powder.

3. Tapped density

It was determined by placing a graduated cylinder, containing a known mass of drugexcipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by

$$D_t = M / V_t$$

Where, M is the mass of powder and Vt is the tapped volume of the powder.

4. Porosity

The porosity € of powder is defined as the ratio of void volume to the bulk volume of the packaging.

The porosity of the powder is given by

$$€ = Vb - Vp / Vp = 1 - Vp/Vb$$

Porosity is frequently expressed in percentage and is given as

$$\%€ = (1 - Vp/ Vb) X 100$$

5. Powder flow properties

The flow properties were determined by

i) Carr's Index (I)

It is expressed in percentage and is expressed by

$$I = D_t - D_b / D_t$$

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

ii) Hausner ratio

It is expressed in percentage and is expressed by

$$H = D_t / D_b$$

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder**.**

Table 3: Evaluation of mouth-Disintegrating tablets of Dicyclomine HCl.

Formulation Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Thickness (mm)	1.6	1.7	1.5	1.6	1.6	1.5	1.7	1.5	1.6
Diameter(mm)	8	8	8	8	8	8	8	8	8
Wt. Variation(mg)	100.01 ± 0.39	102.10 ±0.12	101.48 ±0.19	103.89 ±0.41	101.48 ±0.19	100.01 ±0.39	98.54 ±0.28	103.89 ±0.41	102.10 ±0.12
Hardness (kg/cm2)	6.4	7.0	5.0	8.8	6.0	9.9	8.2	7.0	6.0
Friability(%)	0.42± 0.2	0.40± 0	0.40± 0	0.39± 0	0.39± 0	0.39± 0	0.40± 0	0.40± 0	0.39±0
Water absorption ratio(sec)	39.12 ±4.10	32.58 ±2.45	42.16 ±3.21	42.73 ±5.21	35.45 ±2.45	38.21 ±3.10	36.65 ±2.15	35.45 ±2.45	36.65 ±2.15
***In-vivo* disintegratin time(sec)**	36.0 ±4.12	35.0 ±3.15	36.0 ±4.20	38.0 ±5.30	36.0 ±4.20	38.0 ±6.02	36.0 ±4.20	32.0 ±4.65	33.0 ±6.10
Disintegration Time(sec)	50	45	70	72	75	65	60	65	70
Wetting time (sec)	25	26	25	30	34	26	25	30	32
Solution volume (ml)	1±2	1±3	1±2	1±4	1±2	1±1	1±2	1±3	1±3
Drug Content (mg/tablets)	19.8	19.7	19.8	19.6	19.8	19.7	19.9	20.1	19.7
%Cumulative Release (10 min)	98.42	97.20	96.73	97.35	98.34	97.89	98.27	97.96	97.89

Average of three determinations

Table 4: Comparison of parameters for Batch F5 Initial and after three months

Parameter	Batch F5 (Initial)	Batch F5 (After three month)
Hardness kg/cm^2	6.0	6.2
Friability	0.39±0	0.39±0
Disintegration time (sec.)	75	77
Wetting time (sec)	34	35
Solution Volume(ml)	1±2	1±2
Water absorption ratio(%)	0	±0.16

Table 5: *In Vitro* % Cumulative Release of all formulation

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	98.42	98.19	96.81	97.88	98.57	98.42	98.26	98.34	98.19
10	97.88	97.2	96.73	97.35	98.34	97.89	97.27	97.96	97.89
15	96.44	96.28	95.28	96.29	97.34	96.93	97.12	96.51	96.89
30	89.48	89.48	88.4	95.28	92.85	95.13	94.06	94.07	94.37
45	87.15	86.65	83.33	86.64	86.56	85.12	86.72	86.26	85.72
60	86.3	86.6	80.55	82.02	85.92	83.31	85.69	85.75	85.14

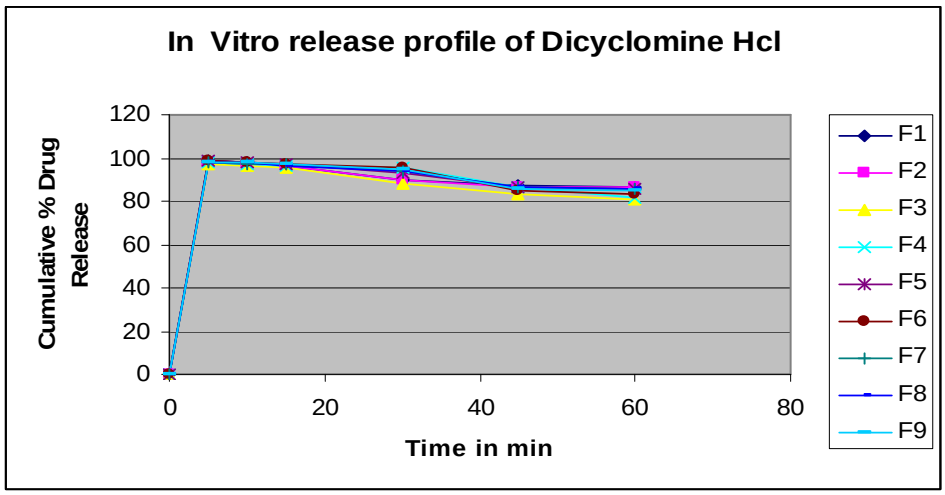


Fig. 1: *In-vitro* release profile of Dicyclomine HCl formulations

Evaluation of the tablets

Thickness and diameter
Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

Hardness [6,7]
The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability [8]
Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula:

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight Variation
Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±4.5% (USP XX).

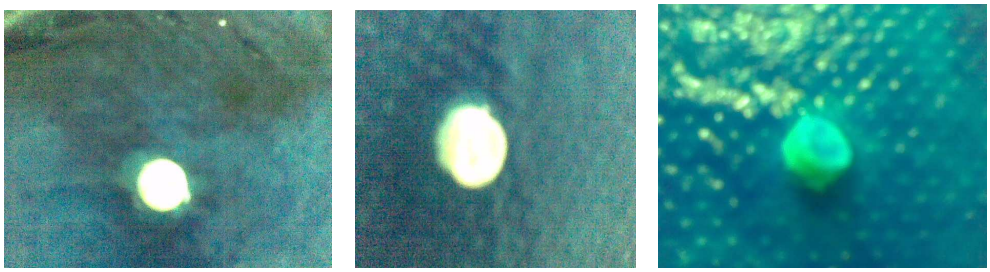
Drug content [9]
Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20mg of Dicyclomine HCl was dissolved in 100ml of pH 6.8 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 214nm using UV-Visible spectrophotometer (UV 160-Shimadzu, Japan).

Content uniformity
Colorimetric measurement of glucomannan in the AVG was used for determining drug content uniformity13. For the drug content, 10 tablets were weighed and triturated. A tablet triturate, equivalent to 2 mg of AVG, was weighed accurately and dissolved in 100 ml of distilled water and filtered. From this solution, 0.4 ml was transferred to a 10 ml test tube. To this, 4 ml of Congo red reagent (0.01 %) was added with mild vortexing. The mixture was left at room temperature for 20 min and absorbance was measured at 214 nm wavelength using UV-VIS spectrophotometer (SL-196, Elico Ltd). The amount of glucomannan was calculated by interpolating from the standard curve .

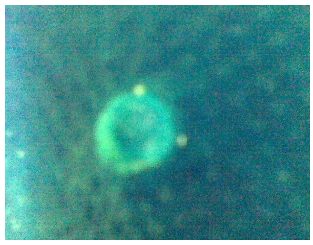
Wetting time [10]
A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 10ml of buffer solution simulating saliva pH 6.8, A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each

formulation were randomly selected and the average wetting time was noted. The results are tabulated in Table 3.

Fig. 7: Images showing wetting time of FDTs.



After 5 sec After 10 sec After 45 sec



After 60 sec

Water absorption ratio [9]

The procedure of water absorption ratio without Rosaline dye powder was followed for determining the water absorption ratio R was determined according to the following equation: R = [(Wa – Wb)/Wb]× 100 where, Wb and Wa were the weights of the tablet before and after use .

Disintegration time[12]

Disintegration time for FDTs was determined using USP disintegration apparatus with SSF (pH 6.8, 900 ml at 37°C) as the disintegrating medium. To comply the test all tablets should disintegrate within 3 minutes.

***In vivo* disintegration time**

Six healthy human volunteers were selected and their written consent was obtained. Each volunteer randomly took one tablet and kept on the tongue. The time taken for complete disintegration of the tablet on the tongue was noted. It is expressed in seconds. After the test, mouth was washed with distilled water. Three trials were performed with 2 days interval, between trials.

Solution volume

For this evaluation take Petri disk and one tablet place in disk then drop wise use water for wet of tablet. Drop is decide the solution volume until tablet is wet.

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***In vitro* dispersion time** [12]

In vitro dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing 6ml of buffer solution simulating saliva fluid (pH 6.8).

***In vitro* dissolution studies**[13]

In vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus, (Labindia Electrolab, Mumbai) at 50rpm. Phosphate buffer pH 6.8 was used as the dissolution media with Samples were withdrawn at different intervals, diluted suitably and analyzed at 214--nm for cumulative temperature maintained at 37±1ºC. drug release using Shimadzu UV-Visible spectrophotometer.

RESULTS AND DISCUSSION

All the Tablets were exhibit in white in color, odorless, smooth surface with zero defects.
Formulated tablets were evaluated for, drug content, weight variation, hardness, friability, disintegration time, solution volume, drug content, %cumulative release (table 2). The average weight of the prepared tablets was found 99.54 to 102.89 mg. A tablets requires certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The hardness of prepared tablet varied from 5.0 to 9.9kg/cm^2 which have satisfactory strength to withstand the mechanical shocks.

The friability of all the formulation was found to be less than 0.4 %. The results shows resistance to loss of weight indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The disintegration time of the tablets was varied from 45 to 75 seconds. The solution volume of all the formulations was about 1.0 ml. The drug content of the formulation was varied from 19.6 to 20.1 mg per tablet. The release found to be at the end of sixty minutes 80.55 to 86.6 %. The formulations F5 shows best release then other formulation. All the formulations showed no significant variation in all the parameters under the test period.

CONCLUSION

Overall, the results suggest that suitably formulated Fast-Disintegrating tablets of Dicyclomine HCl with a super disintergrant (Micro crystalline cellulose or sodium starch glycollate) can be achieved. The tablets exhibited good i*n vitro* dispersion and wetting properties. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

Acknowledgement
The authors are thankful to Meerut Institute of Engineering & Technology for providing necessary facilities to carry out the research work.

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