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FORMULATION AND IN VITRO EVALUATION OF ORAL DISPERSIBLE TABLET OF DICYLOMINE HCL

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ABSTRACT

Dicyclomine HCL is an antispasmodic drug which is widely used in treatment of smooth muscle spasm of the gastrointestinal tract but it undergoes to first pass Metabolism. So that to develop Fast dissolving tablet of Dicyclomine HCL to avoid first pass metabolism and increase bioavailability. This offers a new range of product having desired characteristics and intended benefits. In this research, orally dispersible tablets of Dicyclomine HCL were prepared using direct compression method. Tablets produced by direct compression method contain Lactose as diluent, Crosscarmellose sodium, crosspovidone and husk as a superdisintegrant and aspartame as a sweetener. The dissolution study was performed on PBS 6.8 (salivary pH) and the In-vitro release was found 98.51% without leaving residue for F3 Batch.

KEYWORDS: Fast dissolving tablet, Superdisintegrants, Direct compression, Oral route.

INTRODUCTION

Solid dosage forms like tablet and capsule are most popular and preferred drug delivery system because they have high patient compliance, relatively easy to produce easy to market, accurate dosing, and good physical and chemical stability.[1] Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the food stuffs that are ingested daily. In fact, the development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology. Therefore, a fundamental understanding of various disciplines, including GI physiology, pharmacokinetics, pharmacodynamic and formulation design are essential to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form. In any case, the scientific frame work required for the successful development of an oral drug delivery system consists of a basic understanding of the following three aspects, Physicochemical, pharmacokinetic and Pharmacodynamic characteristics of the drug, The anatomic and physiologic characteristics of the GIT, and Physicochemical characteristics and the drug delivery mode of the dosage form to designed.[2] Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional tablets and capsules. When water is not available, in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic conditions and bronchitis.[3] For these reasons, tablets which can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.[4] Orally disintegrating tablets are also called as oral dispersible tablet, quick disintegrating tablets mouth dissolving tablets. European pharmacopoeia has used the term oral dispersible tablet for tablets that disperse readily and within 3min in mouth before swallowing.[5] Dicyclomine HCL is an antispasmodic drug which is widely used in treatment of smooth muscle spasm of the gastrointestinal tract but it undergoes to first pass Metabolism. So that to develop mouth-dissolving tablet of Dicyclomine HCL to avoid first pass metabolism and increase biosavailability. This offers a new range of product having desired characteristics and intended benefits, to achieve reliable bioavailability and enhance patient compliance. The objective of the present work is too to study the pre formulation factors of Dicyclomine HCL such as solubility, melting point, PH, pka, max standard calibration curve of drug in phosphate buffer pH 6.8. To formulate fast dissolving tablets of Dicyclomine HCL

using superdisintegrants in different ratios by direct compression technique. To study the pre-compression parameters like bulk density, tapped density, angle of repose, carr‟s index and haunser ratio for prepared tablet formulations To evaluate prepared tablets by different post-compression parameters such as thickness, hardness, friability, *in vitro* dispersion time, content uniformity, weight uniformity, wetting time, water absorption ratio and *in vitro* dissolution study. To study *in vitro* dissolution of fast dissolving tablets of Dicyclomine HCL in phosphate buffer pH6.8 solution, Spectroscopy analysis F.T.I.R., U.V. to achieve better patient compliance.[5]

MATERIAL AND METHOD

Dicyclomine HCL was received as a gift sample from Micro Labs Mumbai. Crosspovidone , and Talcam Powder were procured from Loba Chem pvt Ltd Mumbai. Lactose was procured from Merck ltd. Mumbai. Crosscarmellose sodium and Aspartane were procured from Shreeji Chemicals, Mumbai. Microcrystalline Cellulose was procured from LR S D fine chemical Mumbai. Magnesium stearate was procured from Amishi Drug & Chemicals Ahmedabad. Husk (isabgol) was procured from Sidhpur sat- isabgol factory, Gujrat.

Preformulation Studies Fast Dissolving Tablet[6-7]

Preformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance. Preformulation yields basic knowledge necessary to develop suitable formulation for the toxicological use. It gives information needed to define the nature of the drug substance and provide frame work for the drug combination with pharmaceutical excipients in the dosage form. Hence, the following preformulation study of mixed blend done for the flow property of powder that are Micromeritic properties(Bulk density and tapped density) were determined using a bulk density apparatus and Flow properties **(**Angle of repose, compressibility index and Hausner ratio) were evaluated.

Preparation Of Oral Dispersable Tablet Of Dicyclomine Hcl[8]

Tablets containing Dicyclomine HCL were prepared by direct compression method. Dicyclomine HCL fast dissolving tablets were manufacture in nine formulations F1 to F9 using the ingredients keeping the various formulations batches were prepared according to formula. Tablets are compressed directly from powder blends of active ingredient and suitable excipients (including fillers, disintegrants, and lubricants). Drug, directly compressible Lactose, Superdisintegrant (Crosscarmellose sodium, Husk and Crosspovidone), Microcrystalline Cellulose, Aspartame and Talc were mixed together for 20 min. Magnesium stearate, was then added and mixed for 5 min. The powder blend was than mixed well by using mortar and pestle for 15 to 30 minutes, and then each mixture was passed through #80sieve.Tablet were compressed on a single punch tablet machine (Cadmach Single Station) to produce flat faced Dicyclomine HCL weighing 200 mg. (shown in table 1.).

Table 1: Superdisintegrant ratio profile in fast dissolving tablets of Dicyclomine HCL.

Polymer ratio	F1	F2	F3	F4	F5	F6	F7	F8	F9
Crosspovidone									
&	1:2	1.5:3	2:2	-	-	-	-	-	-
Crosscarmellos									
Sodium									
Crosspovidone									
&	-	-	-	1:2	1.5:3	2:2	-	-	-
Husk									
Crosspovidone,									
Crosscarmellos	-	-	-	-	-	-	1:1:1	1.5:1.5:1.5	2:2:2
Sodium & Husk									

Table 2: The formulations composition of fast dissolving tablets of Dicyclomine HCL.

Ingredients	Drug combination ratio, Formulation Code & Quantity (mgs)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
	1:1.5	1:2.25	1:3	1:1.5	1:2.25	1:3	1:1.5	1:2.25	1:1.5
Dicyclomine HCL	20	20	20	20	20	20	20	20	20
Lactose	70	55	40	70	55	40	70	55	40
Crosspovidone	10	15	20	10	15	20	10	15	20
Crosscarmellose	20	30	40	-	-	-	10	15	20
Sodium									
Microcrystalline	60	60	60	60	60	60	60	60	60
Cellulose									

Talcam powder	4	4	4	4	4	4	4	4	4
Magnesium	6	6	6	6	6	6	6	6	6
Stearate									
Aspartame	10	10	10	10	10	10	10	10	10
Husk	-	-	-	20	30	40	10	15	20

Evaluation Parameter Of Oral Dispersable Tablet Of Dicyclomine Hcl

Precompression Parameter[9-10]

1. Angle of repose (θ)

The values were found to be in the range of 20.5^{0} to 29.0^{0}. All formulations showed the angle of repose with in29.0^{0}. It indicates that all formulations showed good flow properties. (Shows in table 3).

2. Bulk Density

The loose bulk density and tapped bulk density for the all formulations varied from 0.52gm/cm^3 to 0.59 gm/cm^3 and 0.60 gm/m^3 to 0.69 gm/cm^3 respectively. The values obtained lies within the acceptable range and not large difference found between loose bulk density and tapped bulk density. This result helps in calculating the % compressibility and hausner's ratio of the tablet blend. (Shown in table 3).

3. Percentage Compressibility

This percent compressibility of tablet blend was determined by carr's Index. The percentage compressibility for the all nine formulations lies within the range of 12.90 to 15.87%.All the formulations showing good compressibility. (Shows in table 3).

4. Hausner's Ratio

This hausner's ratio of tablet blend was determined. The hausner's ratio for the all nine formulations lies within the range of 1.14 to 1.18. All the formulations showing good flow property. (Shows in table 3)

Table 3: Different flow property parameters of Dicyclomine HCL.

Formulations	Angle Of Repose (θ)	Loose Bulk Density (gm/cm3)	Tapped Bulk Density (gm/cm3)	% Compressibility	Hausner's Ratio
F1	26.56	0.54	0.62	12.90	1.14
F2	28.14	0.53	0.63	15.87	1.18
F3	29.00	0.54	0.62	12.90	1.14
F4	25.24	0.59	0.69	14.49	1.16
F5	26.41	0.57	0.66	13.63	1.15
F6	25.12	0.54	0.62	12.90	1.14
F7	20.59	0.55	0.65	15.38	1.18
F8	21.67	0.53	0.62	14.51	1.17
F9	20.50	0.52	0.60	13.33	1.15

5. Swelling index

The values were found to be in the range of 84 & 47. It indicates that Plantago ovata husk and Croscarmellose sodium showed good Swelling property. The results obtained for Swelling index of Plantago ovata husk and Croscarmellose sodium (Shows in table 4)

Table 4: Swelling Index comparison of Natural and semi synthetic Superdisintegrant.

Name of Superdisintegrant	Swelling Index (% V/V)
Plantago ovata husk	84
Croscarmellose sodium	75

Post-compression parameters [11-20]

1. Thickness test:

The thickness of tablets measured by using vernier calipers by picking the 20 tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from 2.91±0.01 mm to 2.97±0.01 mm respectively. (Shows in table 5)

2. Uniformity of weight

The all tablet pass weight variation test and % weight variation was in the Pharmacopoeial limit of ±7.5%.It was found to be from 198.80 to 201.09mg. This is due to good flow property and compressibility in all formulations. (Shows in table 5)

3. Hardness test

Hardness test was performed by Pfizer hardness tester. Hardness was maintained to be 2.5kg/cm2 to 2.7 kg/cm2. The hardness of all formulations were uniform and have sufficient mechanical strength. (Shows in table 5)

4. Friability test

The study result was found in well approved range (<1%) in all formulations. Result revealed that the tablets posses good mechanical strength. (Shows in table 5)**.**

Table 5: The Evaluation parameters of Dicyclomine HCL tablets.

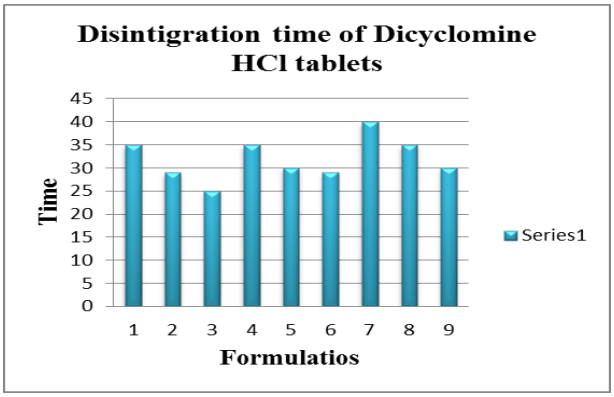
Formulations	Hardness (kg/cm2)	Friability (%)	Weight Variation	Water Absorption Ratio
F1	2.6	0.7	199.10±0.20	100.00±0.06
F2	2.5	0.8	201.09±0.33	106.06±0.91
F3	2.5	0.7	200.19±0.21	109.06±0.03
F4	2.6	0.6	200.33±0.76	92.20±0.09
F5	2.7	0.7	198.80±0.34	86.30±0.03
F6	2.6	0.7	200.33±0.12	97.44±0.26
F7	2.7	0.7	199.60±0.28	115.00±054
F8	2.6	0.5	200.43±1.27	105.06±0.23
F9	2.7	0.6	199.26±0.20	119.53±0.31

5. Water Absorption Ratio

The ratio values of formulations found in the range of 86.30 to 119.53. The water absorption ratio for all formulations shows in table no5.

6. *In vitro* Disintegration time study

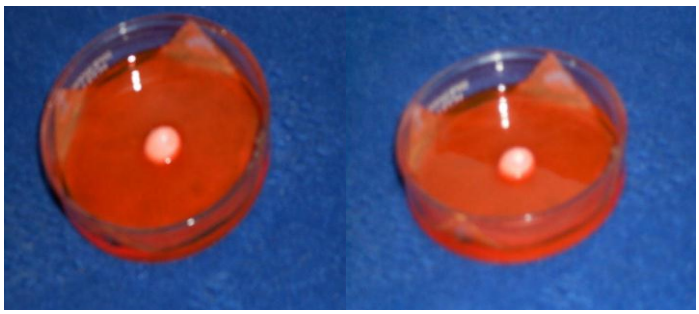
The internal structure of tablet that is pore size distribution, water penetration into the tablet and swelling of disintegrating substance are suggested to be the mechanism of disintegration. The all formulation showed disintegration time less than 40 sec. Disintegration time was observed in the order of crosscarmellose sodium > husk. The study shown in table no.5 & Figure. no.1.



Figure; 1in vitro disintegration study of dicyclomine hcl tablets (f1-f9)

7. Wetting Time

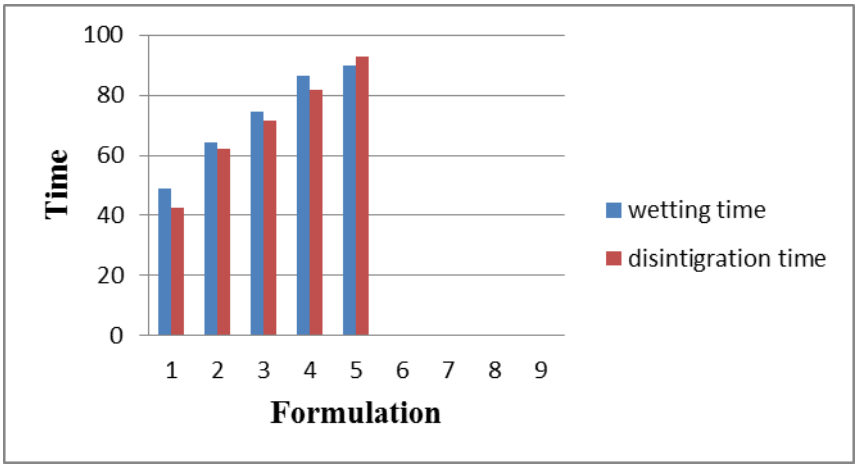
Wetting time depend upon inner structure of tablet and hydrophilicity of excipients. The record of wetting time was shown in Table no. 6.The wetting time in the all formulations is very fast.



Figure; 2 wetting time study of dicyclomine hydrochloride tablets

Table; 6 wetting time and disintegration time (sec) study of dicyclomine hydrochloride tablets.

Formulations	Wetting time(sec)	Disintegration time(sec)
F1	35	25
F2	29	23
F3	25	20
F4	35	26
F5	30	22
F6	29	21
F7	40	30
F8	35	27
F9	30	24



Figure; 3 Disintegration time vs wetting time study of Dicyclomine hydrochloride tablets (F1-F9).

8. Uniformity Drug Content

The drug content of uniformity nine formulations was study. the % drug content deviation was calculated & found the result between 92.68 % to 100.74% of Dicyclomine hydrochloride tablets.(show in table no.7)

Table 7: The % drug content deviation of dicyclomine hcl tablets.

Formulation code	% drug content
F1	95.77±0.9
F2	92.68±1.12
F3	98.62±0.50
F4	91.66±0.9
F5	96.49±1.34
F6	86.35±2.45
F7	91.55±1.6
F8	90.11±1.6
F9	92.74±0.93

***9. In Vitro* Dissolution Time Study**

In vitro dissolution studies of the all formulations of Dicyclomine Hydrochloride were carried out in 6.8 pH phosphate buffer. Percentage drug release was calculated at time interval 3, 6, 9, 12 and 15 minutes. The variation in % drug release was due to different types of superdisintegrants at different concentrations in the all formulations.Dissolution study revealed that the almost all the drug released within the 15 minutes from the all formulations. From the dissolution data it can be observed that the Formulation F1 containing CP and CCS showed the highest percentage of % drug release (98.51%). This may be occurred due to the higher concentration of superdisintegrants used in the formulation. The formulation batches containing Crospovidone + Croscarmellose sodium showed comparatively higher % drug release than the other batches of the formulation with corresponding concentrations of Superdisintgrants. The study shows in table no.8, 9 &10. Table .no.8 the %cumulative drug release of dicyclomine hcl tablets containing crosscarmellose sodium and crosspovidone.

Table 9: The % cumulative drug release of Dicyclomine HCl tablets containing Hsuk and Crosspovidone.

Sr.no.	Time(min)		% cumulative drug release	
		F1	F2	F3
1	3	48.86	42.67	39.17
2	6	64.45	62.12	56.87
3	9	74.32	71.54	68.40
4	12	86.42	81.78	76.65
5	15	89.62	92.78	98.51

Sr.no.	Time(min)		% cumulative drug release	
		F4	F5	F6
1	3	48.86	42.67	39.17
2	6	64.45	62.12	56.87
3	9	74.32	71.54	68.40
4	12	86.42	81.78	76.65
5	15	97.50	92.15	89.50

Table 10: The % cumulative drug release of Dicyclomine HCl tablets containing Crosscarmellose sodium, husk and Crosspovidone.

Sr. no.	Time(min)	% CUMULATIVE DRUG RELEASE		
		F7	F8	F9
1	3	48.86	49.76	46.82
2	6	63.12	56.87	59.58
3	9	80.42	72.50	75.65
4	12	89.90	84.89	89.64
5	15	92.81	95.00	94.12

RESULT AND DISCUSSION

The formulated fast dissolving tablets of Diyclomine HCL with a superdisintergrant (cosspovidone, crosscarmellose sodium and husk) can be achieved. The tablets exhibited good In vitro dispersion and wetting properties. Thus the present study demonstrated potential for rapid absorption, improved bioavailability, effective therapy and patient compliance. Fast dissolving tablets worked formulated using the different supperdisintegrant such as husk, crosspovidone and crosscarmellose sodium by the direct compression method. The fast dissolving tablets of Dicyclomine HCL showed the excellent tablets evaluations parameters such as weight variation, friability, hardness, disintegration time, tablets size, shape, in- vitro dissolution profile. The study show as the concentration of superdisintegrant increase in the combination the disintegration time is decrease. The combination made from polymers and superdisintegrant provide satisfactory fast dissolving tablet, which have disintegration time less than 31 (sec). The combination made from superdisintegrant (crosscarmellose and crosspovidone) provide better release pattern with less disintegrantion time. We analyzed that the present investigation of fast dissolving tablets of Dicyclomine HCL showed the better % cumulative drug release in series F3 >F4 > F8 > F9 > F7 > F2 > F5 > F1 > F6 and the disintegration time F3 > F6 > F5 > F2 > F9 > F1 > F4 > F8 > F7. The different combination of supperdisintegants polymers showed the drug release profile in the series of F3 > F2 > F1, F6 > F5 > F4 & F9 > F8 > F7.

CONCLUSION

F3 show better release profile and minimum disintegration time (20sec) is the promising concentration of combination .Which can be used for further study and as model formulation.F3 show the better result between the correlation of wetting time and disintegrantion time. The combination made from superdisintegrant (crosscarmellose and crosspovidone) provide better release pattern with less disintegrantion time. Further this combination in the ratio1:3 (drug combination ratio) provide better drug release with (20 sec) shortest disintegration time. So the (1:3) drug combination is the promising concentration of superdisintegrant which provide better release and less disintegration time.

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