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Preparation and Physicochemical Evaluation of Oral Disintegrated Tablet Containing Dicyclomine Hydrochloride

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A B S T R A C T

Dicyclomine hydrochloride is anticholinergic used as an anti-spasmodic drug. The aim of this study was to prepare hard and fast oral disintegrating tablets (ODTs) containing Dicyclomine hydrochloride which can release drug at the least possible time. The ODTs serve as an alternative dosage form for patients who experience dysphagia (difficulty in swallowing) or for increasing the patient compliance. The ODTs were prepared using croscarmellose, crospovidone, and mallow mucilage as superdisintegrants. Tablets formulated by direct compression method and various parameters were evaluated. Based on disintegration time and hardness of tablets, two types of superdisintegrants (mallow mucilage and croscarmelose) selected and different ODTs containing combination of two superdisintegrant were prepared. Angle of repose and Carr's index of tested powders were in the range of 27.3 to 30.1 and 9.3 to 23.91 respectively. These findings indicated that the powder prepared possessed appropriate flow properties. The ODTs of dicyclomine showed uniform content and low weight variation. Friability percent was below 0.8%, which was in acceptable limit. The tablet formulations contained mucilage at concentrations of 3.3-5% in combination with croscarmelose showed lower disintegration time as compared to those containing mucilage alone. Formulation containing 5% mucilage and 3.3% croscarmelose identified as optimum formulation because of lowest disintegration time, acceptable drug release time and appropriate hardness.

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Introduction

Dicyclomine hydrochloride is a tertiary amine used as an antispasmodic drug. It exerts some nonspecific direct relaxant effect on smooth muscle. In therapeutic doses, it decreases spasm of the gastrointestinal tract, biliary tract, ureter and uterus [1]. Drinking water plays an important role in the swallowing of oral solid dosage forms. Sometimes, people experience inconvenience in swallowing conventional tablets and capsules such as water inaccessibility, in case of motion sickness and sudden episodes of coughing during the common cold, allergic conditions, and bronchitis. The orally disintegrating tablets (ODTs) serves as an alternative dosage form for patients who experience dysphagia (difficulty in swallowing) or for where compliance is a known issue and therefore an easier dosage form is needed to ensure that medication usage. Among all age groups, dysphagia is observed in about 35% of the general population, as well as up to 60% of the elderly population [2, 3] and 18-22% of all patients in long-term care [4]. ODTs are gaining prominence as novel drug delivery systems. These are useful in administration of drugs in pediatric and geriatric patients and in patients suffering from dysphagia, leading to improved patient compliance. ODTs also have a faster onset of action than that of tablets or capsules. FDA guidance issued in Dec 2008 is mentioned that ODTs drugs should disintegrate in less than 30 seconds [5].

ODTs can increase bioavailability and proved rapid absorption of drugs through pre gastric absorption of drugs from mouth, pharynx & esophagus as saliva passes down [6]. The possibility of suffocation during oral administration of conventional formulations due to physical obstruction reduced, thus safety increased [7].

Type of superdisintegrants has main influence on disintegration time and dissolution effect [8]. Disintegration time is most important property of ODTs that should be optimized [9]. Sodium starch glycolate, crosscarmellose sodium and crospovidone are commonly used superdisintegrants [10]. Plant products is as an alternative to synthetic products due to local availability, eco-friendly nature and lower costs compared to important synthetic products [11]. Natural gums and mucilage have been widely explored as pharmaceutical excipients, are glutinous substance that mainly consists of polysaccharides, proteins and uranides [12]. *Althaea Officinalis* Mucilage used as superdisintegrant in place of currently marketed synthetic superdisintegrating agents. As primary ingredient, it is cheap, biocompatible, biodegradable and easy to manufacture. Xerostomiais, a common side effect of dicyclomine, can be reduced due to wetting property of mucilage. Study conducted by Viral Shah [13], showed the positive effects of mallow mucilage in ODTs preparation. Combination of supedisintegrants may reduce the disintegration time and dissolution time.

The objective of present study was to prepare hard and fast oral disintegrating tablets of dicyclomine, capable of releasing drug at the least time.

Materials and Methods

Dicyclomine hydrochloride was a gift from Alhavi pharma co, (Tehran, Iran). Croscarmellose sodium, starch glycolate, crospovidone, avicel PH 101, mannitol, sucralose, menthol, talc and magnesium stearate were obtained from Farabi pharmaceutical company.

Extraction of mucilage

The fresh petals of Althaea Officinalis collected, washed with water to remove dirt and debris, and dried. The powdered petals were soaked in water for 5–6 h, boiled for 30 min, and kept aside for 1 h for complete release of the mucilage into water. The material squeezed from an eight-fold muslin cloth bag to remove the marc from the solution. Acetone added to the filtrate to precipitate the mucilage. The mucilage was separated, dried in an oven at a temperature < 50 °C, collected, dried-powdered, passed through a sieve (number 80), and stored for further use in desiccators [13].

Preparation of dicyclomine HCl oral disintegrating tablets

In our preliminary studies, ODTs were prepared using either croscarmelose, crospovidone or mucilage as superdisintegrant at three different concentrations (2, 3.3 and 5%). Nine formulations were prepared using direct compression method keeping the total weight of tablet (150 mg) constant in all formulations. The composition of each formulation is shown in Table 1. All raw ingredients mixed together using glass mortar and pestle, and compressed using a single punch tablet machine. Based on disintegration time and hardness of tablets, two types of superdisintegrants selected and different ODTs containing combination of two superdisintegrant were prepared (Table 2). Design expert software (ver.7.2 USA) was used to evaluate the effect of formulation variable on disintegration time, hardness and times required for 100% release of drug ($Q_{100\%}$). The amount of mucilage and croscarmelose was taken as independent variable. Two factors at three levels were studied and 9 runs were designed using general factorial design. The optimum condition determined by an optimization process to yield a heightened performance.

Table 1. Composition of different formulations of Dicyclomine hydrochloride oral disintegrating tablets containing one superdisintegrant.

Ingredients(mg/tablet)	S1	S2	S3	S4	S5	S6	S7	S8	S9
Dicyclomin	20	20	20	20	20	20	20	20	20
Talc	6	6	6	6	6	6	6	6	6
Starch glycolat	10	10	10	10	10	10	10	10	10
Magnesium stearate	2	2	2	2	2	2	2	2	2
Avicel pH 101	40	40	40	40	40	40	40	40	40
Menthol	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Sucralose	12	12	12	12	12	12	12	12	12
Cross carmelose	3	5	7.5	-	-	-	-	-	-
Cross povidone	-	-	-	3	5	7.5	-	-	-
Musilage	-	-	-	-	-	-	3	5	7.5
Manithol	45.5	43.5	41	45.5	43.5	41	45.5	43.5	41
Total weight	150	150	150	150	150	150	150	150	150

Table 2. Composition of different formulations of Dicyclomine hydrochloride oral disintegrating tablets containing combination of two superdisintegrants.

Ingredients(mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dicyclomin	20	20	20	20	20	20	20	20	20
Talc	6	6	6	6	6	6	6	6	6
Starch glycolat	10	10	10	10	10	10	10	10	10
Magnesium stearate	2	2	2	2	2	2	2	2	2
Avicel pH 101	40	40	40	40	40	40	40	40	40
Menthol	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Sucralose	12	12	12	12	12	12	12	12	12
Musilage	5	5	5	7.5	7.5	7.5	10	10	10
Cross carmelose	5	7.5	10	5	7.5	10	5	7.5	10
Manithol	48.5	46	43.5	46	43.5	41	43.5	41	38.5
Total weight	150	150	150	150	150	150	150	150	150

Evaluation of blends before compression

A. Angle of repose:

Angle of repose was determined by using funnel method. The accurately weighed blend poured in a funnel. The height of the funnel adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The diameter of the powder cone is measured and angle of repose is calculated using the following equation [14,15].

$$\mathbf{Tan\ \theta = h/r}$$

Where h and r are the height of cone and radius cone base respectively. Angle of Repose less than 30 ° shows the free flowing of the material.

Bulk density: Apparent bulk density determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight. Bulk density calculated by using following formula:

Bulk density = Weight of the powder / volume of the packing

Tapped density: It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder allowed falling under its own weight onto a hard surface from the height of 10 cm at 2 seconds intervals. The tapping s continued until no further change in volume noted. Tapped density calculated by using following formula:

Tapped Density = (Weight of the powder / volume of the tapped packing)

Compressibility index: Compressibility Index can be calculated by using following formula [15] :

Compressibility Index (%) = [(TD-BD) X 100] / TD]

Hausner's ratio: A similar index to indicate the flow properties is defined by Hausner's ratio. Hausner's ratio calculated by using following formula:

Hausner's ratio = (Tapped density x 100)/ (Bulk density)

Hausner's ratio <1.25 – Good flow = 20% **compressibility index**

> 1.25 – Poor flow =33% **compressibility index**

B. Evaluation of Tablets:

Hardness test: Hardness of ODTs was determined using the tablet hardness tester. The pressure is required to break the tablet into two halves by compression. Hardness of 10 tablets from each formulation was determined [16].

Weight Variation: Weight variation test performed with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets. The weight variation of less than 7.5% is within acceptable range [16].

Friability test: The friability of a sample of 20 tablets from each formulation was determined using Roche Friabilator. The pre weight tablets placed in plastic chamber of friabilitor and friabilitor was ran for 4 min at 25 rpm. All tablets de dusted and weight [16].

% Friability = [(W1-W2) X 100]/W1

Where, W1= Weight of tablet before test, W2 = Weight of tablet after test

Disintegration test: The disintegration time of a sample of six ODTs from each formulation was determined using tablet disintegration tester. 900 ml of distilled water kept at 37°C used as disintegration fluid. One tablet is placed in each tube and the basket shake at constant rate of 30 cycles/min. The time required for complete disintegration was determined [17].

Wetting time: Five circular tissue papers of 10 cm diameter placed in a petri dish containing 0.2% w/v eosin solution (3ml). A tablet carefully placed on the surface of the tissue paper. The time was required for appearing blue color on the upper surface of the tablet noted as the wetting time [18].

Content uniformity test: Ten tablets weighed and triturated in a pestle- mortar. Powder blend equivalent to weight of one individual tablet taken and drug content was determined using UV-visible spectrophotometer at 218 nm [17].

***In Vitro* dissolution test:** *In vitro* dissolution studies for all formulation studied in phosphate buffer saline (pH 6) at 37±0.5°C. At predetermined time (0.5, 1, 2, 4, 8 and 12 min), 0.8 ml of medium was withdrawn and replaced with fresh dissolution medium. The concentration of drug was determined by spectrophotometr.

Results and Discussion

Mucilage obtained from Mallow flowers was equal to 10% of the weight of the petals which showed a 17 times increase in volume after absorbing water. The flow properties of mixed powders were evaluated in term of Carr،s index, angle of repose and Hausner ratio. The results are shown in Table 3 and 5. The result for angle of repose and compressibility indexed from 27.3 to 30.1 and 9.3 to 23.91 respectively indicated the good flow properties of powder. This further confirmed by Hausner ratio. The ODTs of dicyclomine prepared using single superdisintegrant. The result of different physicochemical characteristics of tablets is shown in Table 4. The ODTs of dicyclomine showed uniform content and low weight variation. Friability percent was below 0.8% that is in acceptable limit range. In almost all formulations, approximately 100% of drug released within 5 min (Figure.1). Disintegration time of ODTs containing superdisintegrant at 3 concentrations of 2 (3mg), 3.3 (5 mg) and 5 (7.5 mg) percent, were analyzed. The disintegration time of tablets was between 28-31.67(sec) for croscarmelose, 22-42.67 (sec) for crospovidone and 26.33-47.67(sec) for mucilage. Both croscarmelose and mucilage at concentration of 5% showed significantly lower disintegration time and higher hardness (p value<0.05). Mucilage and croscarmelose selected for further study and the effect of different combination of superdisintegrant evaluated. Given the fact that the desirable hardness for tablets is between 30 to 40 N, the results obtained from crospovidone were not acceptable. Computer optimization process by design expert software and a desirability function determined the effect of the levels of independent variables (the amount of mucilage and croscarmelose) on the responses (disintegration time, hardness and $Q_{100\%}$). All responses fitted to linear models. The constraint of disintegration time was 21-39 (sec) with targeting on minimum values. Hardness was between 29-37 (N) with the target was set on highest value, and the constraint of release time was between 4 to 6 (min) while target was on minimum. Optimization carried out by design expert software by desirability of 0.6. According to studied factors, formulations containing 5% mucilage and 3.3% croscarmelose identified as optimized formulation because of lowest disintegration time, appropriate hardness and lowest release time. The tablet formulations contained mucilage at concentration of 3.3-5% in combination with croscarmelose showed lower disintegration time as compared to those containing mucilage alone. However, at higher concentration of mucilage disintegration time increased. In a parallel line, Moghimipour, et al [19] showed that increasing the mucilage concentration in the formulations increases disintegration time. This may be explained with formation of viscose gel layer with mucilage. This layer forms a thick layer that hindered the penetration of water [20]. As a results, the disintegration time and releasing time increased. According to figure 3, increasing mucilage content from 5 mg to 7.5 mg increases the hardness. However, at higher amount of mucilage such as 10 mg, the

hardness decreases. Increasing the croscarmelose content also decreases the hardness (figure 3). Figure 4 showed the interaction of croscarmelose and mucilage on tablet hardness. As can be seen in figure 4, a mixture of these two substances follows a pattern similar to that of mucilage (Figure 3) which shows that mucilage affects the hardness at a higher rate compared to croscarmelose. The reason behind increase in hardness by increasing the Mallow content from 5 mg to 7.5 mg might be the adhesive properties of mucilage which reaches saturation at higher concentrations, resulting in lowering the hardness. As can be seen in figure 5, increasing Mucilage content from 5 to 7.5 mg significantly decreases the disintegration time while at higher concentrations, there is a sharp increase in disintegration time due to increase in medium consistency and formation of a gel layer. The same process also happens for croscarmelose. However, due to weaker gel properties of croscarmelose, increasing croscarmelose concentration from 7.5 mg to 10 mg still decreases the disintegration time with a lower slope (Figure 5).

Table 3. Evaluation of pre compression parameters for various batches of ODTs containing one superdisintegrant.

Formulation No.	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose	Hausners Ratio	Carrs Compressibility Index (%)
S1	0.37±0.07	0.46±0.09	29.3±1.24	1.24±0.19	19.57±1.1
S2	0.37±0.06	0.44±0.08	31±1.34	1.19±0.15	15.91±0.95
S3	0.38±0.07	0.43±0.07	28.1±1.23	1.13±0.09	11.63±0.69
S4	0.38±0.08	0.48±0.11	30.2±1.25	1.26±0.27	20.83±1.26
S5	0.35±0.05	0.46±0.09	28.6±1.24	1.31±0.23	23.91±1.12
S6	0.38±0.08	0.45±0.08	29.4±1.25	1.18±0.16	15.56±0.84
S7	0.38±0.08	0.44±0.07	30.1±1.26	1.16±0.13	13.64±0.78
S8	0.38±0.7	0.45±0.07	29.4±1.24	1.18±.015	15.56±1.21
S9	0.38±0.08	0.47±0.08	28.2±1.18	1.24±0.20	19.15±1.66

Table 4. Evaluation of post compression parameters for various batches of ODTs containing one superdisintegrant

Formulation No.	Hardness (N)	Friability (%)	Weight Variation (%)	Disintegration Time (sec)	Wetting Time(sec)	Content Uniformity (mg)	$Q_{100\,\%}$ (min)
S1	30.1±2.12	0.8±0.13	99.6±3.11	29.33±2.41	31±2.01	19.1±1.45	5±0.61
S2	33.2±1.89	0.33±0.09	99.9±2.60	31.67±1.62	35±2.35	19.6±1.55	6±0.59
S3	38.1±1.94	0.52±0.18	102±4.18	28±2.01	28±1.98	20±1.23	5±0.48
S4	32.3±2.35	0.31±0.07	102.9±2.05	42.67±2.47	45±2.36	19.7±1.21	6±0.60
S5	28.9±1.86	0.46±0.07	98.5±2.53	22.33±1.86	30±2.13	20.01±2.16	4±0.42
S6	36.7±2.47	0.62±0.06	99.5±3.76	33.33±2.35	36±1.79	19.5±2.11	5±0.46
S7	34.1±2.01	0.42±0.08	101±2.53	47.67±2.68	46±2.38	19.8±1.82	6±0.54
S8	31.6±1.62	0.35±0.06	101.3±2.76	39.67±2.12	47±2.08	20.02±2.06	4±0.37
S9	37.2±2.41	0.39±0.11	102.7±2.81	26.33±1.86	31±1.73	19.6±1.98	5±0.41

$Q_{100\,\%}$: Times required for 100% release of drug

Table 5. Evaluation of pre compression parameters for various batches of ODTs containing combination of two superdisintegrants.

Formulation No.	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose	Hausners Ratio	Carrs Compressibility Index (%)
F1	0.38±0.07	0.44±0.09	28.6±1.18	1.16±0.21	13.6±1.10
F2	0.36±0.06	0.45±0.08	30±1.33	1.25±0.20	20±0.9
F3	0.38±0.07	0.44±0.06	27.3±0.98	1.16±0.24	13.6±1.02
F4	0.38±0.05	0.45±0.11	29.9±1.29	1.18±0.19	15.6±1.19
F5	0.39±0.08	0.43±0.06	30.1±1.46	1.1±0.18	9.3±0.82
F6	0.37±0.06	0.44±0.07	29.5±1.37	1.19±0.23	15.9±0.96
F7	0.38±0.07	0.44±0.08	30±1.48	1.16±0.27	13.6±1.10
F8	0.38±0.07	0.43±0.08	28.1±1.25	1.13±0.22	11.6±1.06
F9	0.39±0.08	0.43±0.09	29.8±1.16	1.1±0.19	9.3±0.79

Table 6. Evaluation of post compression parameters for various batches of ODTs containing two superdisintegrant.

Formulation No.	Hardness (N)	Friability (%)	Weight Variation (%)	Disintegration Time (sec)	Wetting Time (sec)	Content Uniformity (mg)	$Q_{100\,\%}$ (min)
F1	33±2.12	0.41±0.05	100.1±1.84	39±2.01	45±2.46	19.8±1.45	6±0.52
F2	32±2.01	0.48±0.08	100.6±2.12	23±1.27	33±1.68	20.02±1.86	6±0.56
F3	31±2.24	0.61±0.09	100.4±1.76	21±1.12	31±1.59	20±1.48	5±0.46
F4	35±2.31	0.43±0.06	100.1±1.82	25±1.56	35±1.94	19.91±1.75	5±0.41
F5	33±1.97	0.45±0.06	99.9±1.91	38±1.95	43±2.41	20.01±1.62	6±0.61
F6	37±2.44	0.32±0.04	99.9±1.99	24±1.44	34±2.08	20.01±1.73	6±0.58
F7	33±1.87	0.43±0.07	100.2±1.96	28±2.03	38±2.12	19.8±1.61	4±0.32
F8	29±1.62	0.82±0.11	98.2±1.76	31±1.97	40±2.21	19.5±2.01	5±0.49
F9	34±2.16	0.38±0.05	100.4±2.04	29±1.76	37±2.73	20.09±1.56	5±0.42

$Q_{100\,\%}$: Times required for 100% release of drug

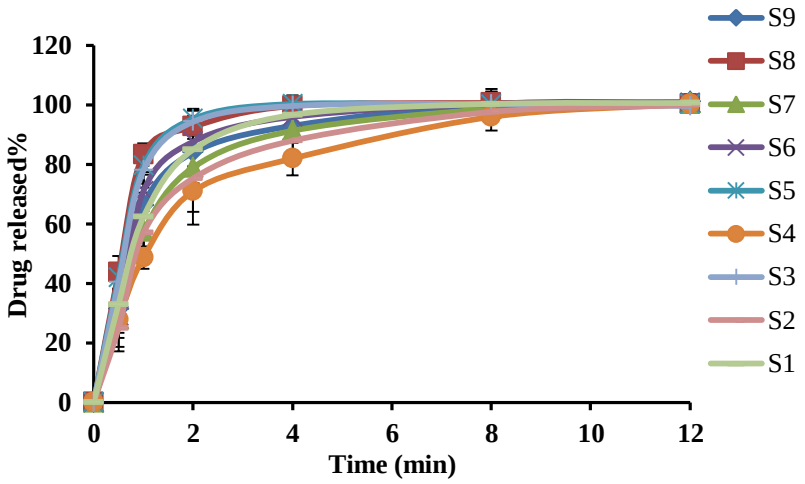

Fig. 1. Drug release curve for ODTs containing one superdisintegrant.

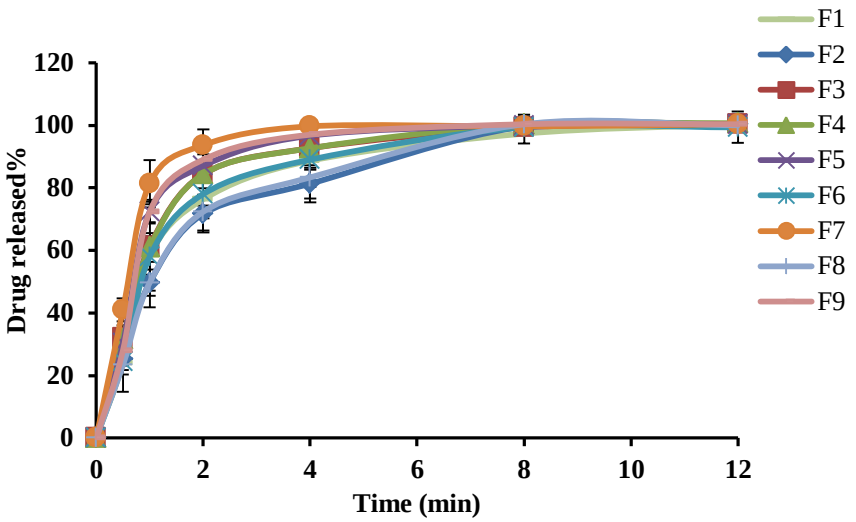

Fig. 2. Drug release curve for ODTs containing combination of two superdisintegrants.

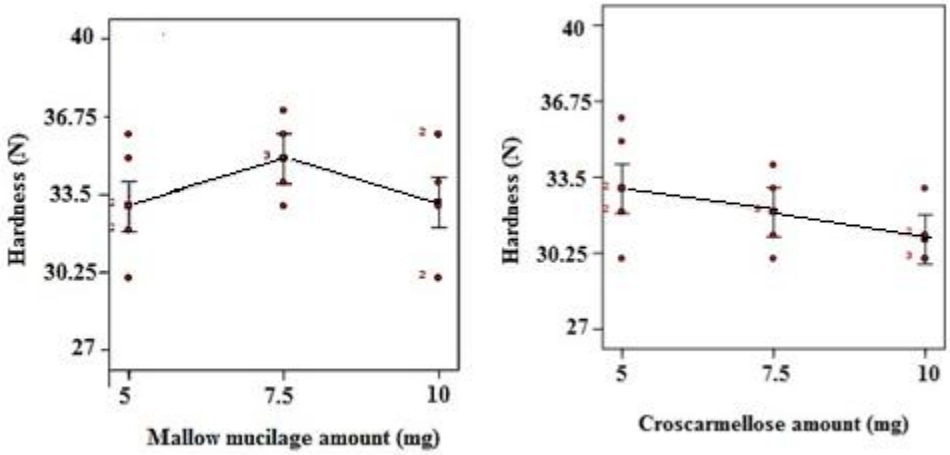

Fig. 3. Effect of different amount of superdisintegrant on tablet hardness.

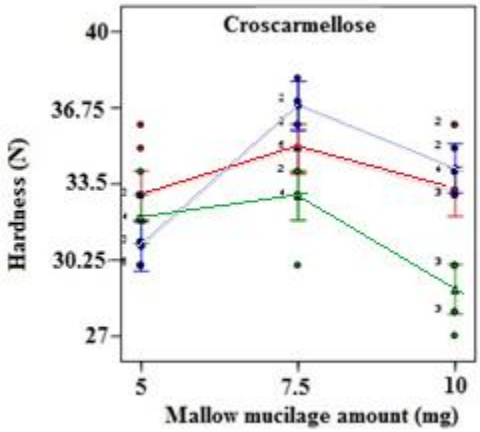

Fig. 4. Effect of interaction of croscarmelose and mucilage on tablet hardness.

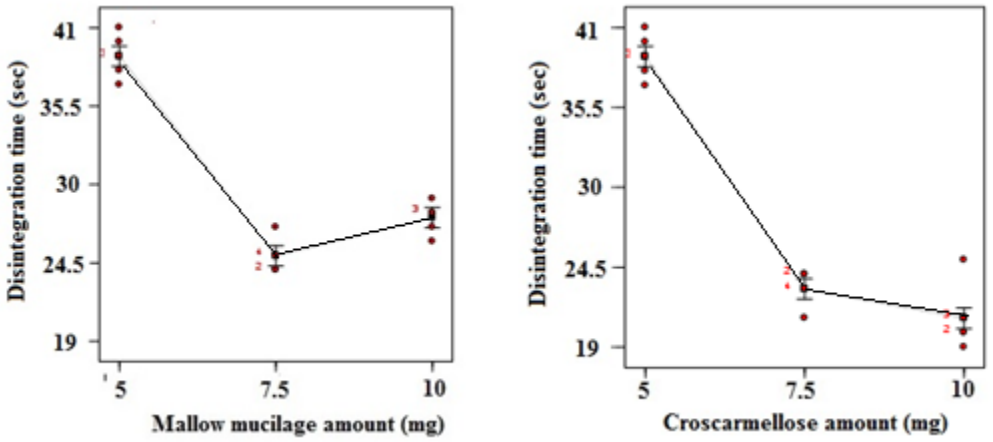

Fig. 5. Effect of different level of mucilage and croscarmellose on tablet disintegration time.

Conclusion

ODTs of dicyclomine hydrochloride prepared successfully by direct compression method using croscarmellose sodium and mucilage from *Althaea Officinalis* as superdisintegrant. The tablets evaluated for pharmacopoeial and non-pharmacopoeial tests. Thus ODTs of dicyclomine hydrochloride were formulated to improve bioavailability and patient compliance. According studied factors, formulation containing 5% mucilage and 3.3% croscarmelose (F4) was identified as optimum formulation because of lowest disintegration time, and drug release and appropriate hardness.

Acknowledgments

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Conflict of interest

Authors certify that there is no actual or potential conflict of interest in relation to this article.

References

[1] Brunton LL, Lazo JS, Parker KL, editor. The pharmacological basis of therapeutics. New York: McGraw-Hill; 1996.
[2] Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery–a review. Pharm Sci Technolo Today. 2000;3:138-145.
[3] Groher ME, Bukatman MS. The prevalence of swallowing disorders in two teaching hospitals. Dysphagia. 1986;1:3-6.
[4] Layne KA, Losinski DS, Zenner PM, Ament JA. Using the Fleming index of dysphagia to establish prevalence. Dysphagia. 1989;4:39-42.
[5] Jain D, Amul M. A Review-Formulation & Development of Orodispersible Tablet. IJPE. 2014;4:21-38.
[6] Parkash V, Maan S, Deepika SK, Hemlata VJ. Fast disintegrating tablets: Opportunity in drug delivery system. J Adv Pharm Technol Res. 2011;2:223.
[7] Kolhe S, More D. Updated review on orally disintergarting tablets: Advancement in current trends. Research Journal of Science and Technology. 2013;5:404-411.
[8] Rojas J, Guisao S, Ruge V. Functional assessment of four types of disintegrants and their effect on the spironolactone release properties. AAPS PharmSciTech. 2012;13:1054-1062.
[9] Ibrahim MA, Amal El Sayeh F. Optimized furosemide taste masked orally disintegrating tablets. Saudi Pharm. J. 2017 .
[10] Desai PM, Er PX, Liew CV, Heng PW. Functionality of disintegrants and their mixtures

[11] in enabling fast disintegration of tablets by a quality by design approach. AAPS PharmSciTech 2014;15:1093-104.

[12] Kamalpreet S, Avninder M, Bharpur S, Gagan S. Studies on mucilage from Acacia nilotcia fruits as suspending agent and binding agent. Int J PharmTech Res. 2014;6:1762-1767.

[13] Alam MT, Parvez N, Sharma PK. FDA-Approved natural polymers for fast Dissolving Tablets. Journal of pharmaceutics 2014;2014.

[14] Shah V, Patel R. Studies on mucilage from Hibuscus rosasinensis linn. as oral disintegrant. Int J App Pharm. 2010;2:18-21.

[15] Bahri-Najafi R, Mostafavi A, Tavakoli N, Taymouri S, Shahraki MM. Preparation and in vitro-in vivo evaluation of acyclovir floating tablets. Res Pharm Sci. 2017;12:128.

[16] Bahri-Najafi R, Tavakoli N, Taymouri S, Shokatjalil S. Gastric floating matrix tablets of metformin hcl: design and optimization using combination of polymers JRPS. 2016;5:67-79.

[17] Battu SK, Repka MA, Majumdar S, Rao Y M. Formulation and evaluation of rapidly disintegrating fenoverine tablets: effect of superdisintegrants. Drug Dev Ind Pharm 2007; 33:1225-1232.

[18] Aslani A, Beigi M. Design, formulation, and physicochemical evaluation of montelukast orally disintegrating tablet. Int J Prev Med. 2016;7:120

[19] Basu B, Bagadiya A, Makwana S, Vipul V, Batt D, Dharamsi A. Formulation and evaluation of fast dissolving tablets of cinnarizine using superdisintegrant blends and subliming material. J Adv Pharm Tech Res. 2011;2:266.

[20] Moghimipour E, Aghel N, Adelpour A. Formulation and characterization of oral mucoadhesive chlorhexidine tablets using Cordia myxa Mucilage. JUNDISHAPUR J NAT PHARM PROD. 2012;7:129.

[21] Bhardwaj TR, Kanwar M, Lal R, Gupta A. Natural gums and modified natural gums as sustained-release carriers. Drug Dev Ind Pharm. 2000;26:1025-38.

