International Journal of Preventive Medicine

Original Article Open Access

Design, Formulation, and Physicochemical Evaluation of Montelukast Orally Disintegrating Tablet

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How to cite this article: Aslani A, Beigi M. Design, formulation, and physicochemical evaluation of montelukast orally disintegrating tablet. Int J Prev Med 2016;7:120.

ABSTRACT

Background: Orally disintegrating tablets (ODTs) are a modern form of tablets that when placed in the oral cavity, disperses rapidly. These tablets have advantages, particularly good applications for children and old patients who have a complication in chewing or swallowing solid dosage forms. The aim of this study was to design, formulate, and evaluate the physicochemical properties of 5 mg montelukast ODTs for the prevention of asthma and seasonal allergies.

Methods: Formulations were prepared with different amounts of super disintegrating agents and effervescent bases as disintegrant agents. Flowability and compressibility of mixed powders were evaluated. The prepared formulations were tested for hardness, thickness, friability, weight variation, drug content, wetting time, disintegration time, dissolution study, and moisture uptake studies.

Results: The compressibility index and angle of repose were in the range of 15.87%–23.43% and 32.93–34.65, respectively. Hardness, thickness, friability, wetting time, and content uniformity of formulations were in the range of 33.7–37.1 N, 3.00–3.81 mm, 0.27%–0.43%, 31–50 s and 96.28%–99.90%, respectively. Disintegration time of the tablets prepared with super disintegrating agents, effervescent bases, and combination of two were in the range of 30–50, more than 60 and 20–36 s, respectively.

Conclusions: Mixture of powders and tablets passed all the specified tests. The results showed formulations prepared by super disintegrating agents and super disintegrating agents with effervescent bases had shorter disintegration time compared to formulations with effervescent bases alone.

Keywords: Direct compression, montelukast, orally disintegrating tablets, prevention of asthma or seasonal allergic

INTRODUCTION

Recent developments in the pharmaceutical industry have prompted scientists to develop new drug delivery systems such as orally disintegrating tablets (ODTs) for improving patient agreement. ODTs without chewing and need to take water, disintegrate, or dissolve quickly in the mouth cavity.[1] The United States Food and Drug Administration Center for Drug Evaluation and Research enrolled a regulation which statuses ODTs as "a solid dosage form containing medicinal substances, which

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DOI: 10.4103/2008-7802.193097

disintegrates rapidly, usually within a few seconds, when located on the tongue."[2] ODTs provide advantages, especially for psychological patients, elderly, and children who have a problem in chewing or swallowing conventional tablets and capsules or pediatric patients with underdeveloped muscular and nervous control that may suffer from ingestion problems.[3,4] Moreover, ODTs are suitable for patients who may be in trip, with little or no access to water and with continuous nausea.[5] The result of decrease in disintegration time of tablet cause to fast dissolution and rapid absorption which prepare rapid beginning of clinical effect.[6] Pregastric absorption of drugs from the mouth may show increased oral bioavailability.[7] ODTs formulations prepare satisfactory stability, simple manufacturing, precise dosing, small size packing, and relaxed handling by patients.[8] ODTs consist of wide variety of medicinal active agents covering many therapeutic categories. The disintegration time of ODTs is usually considered to be <1 min although in most cases, the tablets are disintegrated within 5–30 s. ODTs are specified by low density, hardness, and high porosity.[9-12] To prepare ODTs, various technologies such as direct compression, spray drying, freeze drying, and tablet molding were used.[13]

Montelukast sodium inhibits the cysteinyl leukotriene receptor and is a selective antagonist of leukotriene receptor that used as an alternative to anti-inflammatory medications in the prevention and chronic medication of asthma, exercise-induced bronchospasm, and to relief symptoms of seasonal allergies. It is usually administered orally. Montelukast sodium is a white to off-white colored powder, and it is freely soluble in ethanol, methanol, water, and practically insoluble in acetonitrile. The mean oral bioavailability of montelukast is 64% and more than 99% bound to plasma proteins. Montelukast is extensively metabolized in the liver with cytochromes P450 3A4 and 2C9. Montelukast sodium is available in various dosage forms such as 10 mg film-coated tablet, 4 and 5 mg chewable tablets, and 4 mg oral granules sachet.[14-16] A solution of montelukast when exposed to sunlit showed instability and lead to the creation of its cis-isomer as the main photolized product.[17]

The aim of this study was to design, formulate, and evaluate the physicochemical properties of 5 mg montelukast ODTs to decrease disintegration time of tablet in the oral cavity and hence to improve patient compliance for prevention of asthma and seasonal allergies.

METHODS

Materials

The pharmaceuticals including montelukast sodium were provided from Cobeldarou Pharmaceutical Company (Tehran, Iran). The super disintegrants such as crospovidone (CP), sodium starch glycolate (SSG), and croscarmellose sodium (CCS) and flavoring agents were provided from Farabi Pharmaceutical Company (Isfahan, Iran). Citric acid, sodium bicarbonate, tartaric acid, mannitol, microcrystalline cellulose, aspartame, sodium lauryl sulfate (SLS), magnesium stearate, and polyethylene glycol 6000 were purchased from Merck Company (Germany).

Spectrophotometric analysis

Different aliquots (0.5–8 ml) of a standard solution containing 40 μg/ml montelukast sodium were moved into sequences of 10 ml volumetric containers, and they were diluted with 0.5% of SLS in water. Determination of montelukast sodium was done by spectrophotometry (Shimadzu UV-1240 model) at 346 nm.[18] This experiment was repeated three times a day in 3 consecutive days.

Preformulation

At first, some initial formulations were prepared based on a range of values of super disintegrating agents such as CCS, SSG, and CP and some initial formulations were made up with different amounts of effervescent components such as citric acid, tartaric acid, and sodium bicarbonate [Tables 1 and 2]. Lower amounts of super

Table 1: Initial formulations of montelukast orally disintegrating tablets with various percent of super disintegrants

Formulations	Disintegrant	Disintegrant (%w/w)	Disintegration time (s)
S_1	SSG	2	120
S_2	SSG	5	50
S_3	SSG	8	50
S_4	CCS	0.5	71
S_5	CCS	2.5	47
S_6	CCS	5	35
S_7	CP	2	42
S_8	CP	3.5	37
S_9	CP	5	14

SSG=Sodium starch glycolate, CCS=Croscarmellose sodium, CP=Crospovidone

Table 2: Initial formulations of montelukast orally disintegrating tablets with various ratios of effervescent bases

Formulations	Citric acid	Na bicarbonate	Tartaric acid	Disintegration time (s)
E_1	1	3.4	2	72
E_2	1	3.4	1	71
E_3	1	3.4	1.5	74
E_4	1	1.7	1	73
E_5	1	1.7	0.5	82
E_6	-	3.4	1	75
E_7	1	3.4	-	74
E_8	1	1.7	-	70
E_9	2	3.4	-	65

disintegrating agents which had disintegration time under 1 min were screened out and used for the final formulations of tablets for combination whether together or with effervescent bases which had lowest disintegration time.

Evaluation of powder mixture

The angle of repose, compressibility index, and Hausner's ratio characterized the flowability properties of blended powders before compression.

Angle of repose (θ)

Angle of rest is an index of the frictional forces in a powder blend. It is determined as the most possible angle that powder mass created by the horizontal plane. The pile of blend was permitted to flow to a stand at a fixed height through a cone fixed. By measuring the height (H) and diameter (D) of the formed powder mass and putting the values into the formula, the angle of repose (θ) was calculated:[19]

$$\text{Tan } \theta = (2H/D) \quad \text{Eq. (1)}$$

Compressibility index

The compressibility index is evaluated by measured values for bulk density (ρ_b) and tapped density (ρ_t) of mixed powder. The compressibility index percentage was computed as:[19,20]

$$\text{compressibility index} = \frac{\rho \text{ tapped} - \rho \text{ bulk}}{\rho \text{ tapped}} \times 100 \quad \text{Eq. (2)}$$

In these equations, ρ tapped and ρ bulk are:

$$\rho \text{ bulk} = \frac{m}{\text{V bulk}} \quad \text{Eq. (3)}$$

$$\rho \text{tapped} = \frac{m}{\text{V tapped}} \quad \text{Eq. (4)}$$

m: Initial weight of powder,

V bulk: Initial volume of powder before hitting,

V tapped: Second volume of powder after hitting.[19]

Hausner's ratio

Hausner's ratio indicates the flow property of mixed powders. This ratio can be measured by the next equation:[19,21]

$$\text{Hausner's ratio} = \frac{\rho \text{ tapped}}{\rho \text{ bulk}} \quad \text{Eq. (5)}$$

Tablets preparation

By direct compression technique, montelukast ODTs were prepared by effervescent and super disintegrants bases. According to Tables 3 and 4, materials of each formulation were weighed and then montelukast sodium was added to each formulation. Fruit flavoring agents were added to formulations for evaluating taste. Finally, after preparation of appropriate mixture, lubricant was added. Then, the ingredients were mixed in the geometrical method; they were compressed into tablets using 8 mm round flat punches (Kilian and Co., Germany).

Table 3: Ingredients for final formulations of montelukast orally disintegrating tablets with super disintegrants and their mixtures

Ingredients (mg)	Formulations					
	S_2	S_5	S_7	S_2S_5	S_2S_7	S_5S_7
Montelukast sodium	5.2	5.2	5.2	5.2	5.2	5.2
SSG	6	-	-	6	6	
CCS	-	3.75	-	3.75	-	3.75
CP	-	-	3	-	3	3
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5
Aspartame	5	5	5	5	5	5
MCC	30	30	30	30	30	30
Mannitol	99.3	101.55	102.3	95.55	96.3	98.55
Total weight	150	150	150	150	150	150

SSG=Sodium starch glycolate, CCS=Croscarmellose sodium, CP=Crospovidone, MCC=Microcrystalline cellulose

Table 4: Ingredients for final formulations of montelukast orally disintegrating tablets with mixture of super disintegrants and effervescent bases

Ingredients (mg)	Formulations					
	E_8S_2	E_9S_2	E_8S_5	E_9S_5	E_8S_7	E_9S_7
Montelukast sodium	5.2	5.2	5.2	5.2	5.2	5.2
Na bicarbonate	16	32	16	32	16	32
Citric acid	9	18	9	18	9	18
SSG	10	10	-	-	-	-
CCS	-	-	5	5	-	-
CP	-	-	-	-	4	4
Magnesium stearate	2	2	2	2	2	2
PEG 6000	4.6	4.6	4.6	4.6	4.6	4.6
Aspartame	5	5	5	5	5	5
MCC	40	40	40	40	40	40
Mannitol	108.2	83.2	113.2	88.2	114.2	89.2
Total weight	200	200	200	200	200	200

SSG=Sodium starch glycolate, CCS=Croscarmellose sodium, CP=Crospovidone, MCC=Microcrystalline cellulose, PEG=Polyethylene glycol

Physicochemical evaluation of the prepared tablets

Weight variation

Twenty tablets were randomly selected and weighed individually, and the mean weight was calculated. In this test, not more than two tablets should have a deviation greater than pharmacopeia limits (±7.5% of the weight tablet).[22,23]

Friability test

Ten tablets were weighed and placed in the friabilator machine (Erweka, TAP, Germany). This instrument was installed on Erweka motor and turned on the speed of 25 rpm for 4 min. The segregated particles of the tablets

were carefully removed, and tablets were reweighed. Friability percentage was obtained from the following equation.[23]

$$\frac{\text{Initial weight of the tablets} - \text{Final weight of the tablets}}{\text{Initial weight of the tablets}} \times 100 \quad \text{Eq. (6)}$$

Thickness test

In this test, thickness of ten tablets was randomly measured by a vernier caliper (For-Bro Engineers, India). The variation range of thickness should not be out of 5% of normal standard.[23]

Hardness test

Hardness of ten tablets was checked individually using hardness equipment in N scale (Erweka, 24-TB, Germany) In ODTs, this value was generally less than formal tablets.[23]

Assay

Twenty tablets were weighed and comminuted. The powder equal to one tablet was considered exactly and in 25 ml of SLS 0.5% in water dissolved. The consequent solution was filtered by filtration paper and then the following dilutions were carried out. The diluted solution absorbance was calculated from the consequent equation of the montelukast in SLS 0.5% in water at 346 nm.

Content uniformity

Ten tablets selected by chance, then the content of each pill was measured distinctly.[18]

In vitro disintegration time

The test was carried out on six tablets using the fixed basket containing six cylindrical glass tubes, the bottom of each tube is connected to a stainless steel basket with certain mesh. The disintegration media was purified water at 37°C ± 2°C and the time that disintegration of the tablet was completed in the apparatus was recorded in seconds.[24]

Wetting time

A piece of twice-folded tissue paper was put into 6 ml of water in a Petri dish. A pill was located on the tissue paper, when wetting was completed the time recorded.[25]

Dissolution test

Montelukast sodium ODTs dissolution test was carried out with United State Pharmacopeia (USP) dissolution apparatus Type II (paddle) at 50 rpm with dissolution medium of SLS 0.5% in purified water at 37°C ± 0.5°C.[26] At times of 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 min, 5 ml sample was removed and substituted by new media. The concentration of samples was measured by ultraviolet (UV) spectrophotometry (Shimadzu UV-1240 model) at 346 nm.

Evaluation of flavor of the prepared tablets

To evaluate the taste, panel tests performed by the Latin square method. At first, formulations were prepared with various flavoring agents such as cherry, tutti-frutti, orange, and without flavor but the same amounts of sweeteners and the same content of active drug and excipients. Twenty healthy volunteers were selected and divided into four groups: The first group was given cherry (A), tutti-frutti (B), orange (C), and without flavoring agents (D). The second group: B, C, D, and A; third: C, D, A, and B; and the fourth group was the D, A, B, and C. Then, the volunteers were asked to score each of the formulation from 1 to 5 (1: bad, 2: poor, 3: average, 4: good, and 5: very good taste).[27]

Moisture uptake study

Moisture uptake studies for ODTs provide some good information of formulation stability; therefore, moisture uptake study is an important study in the case of ODTs.

Moisture uptake studies were carried out by weight method. For complete drying of the tablets, ten tablets were kept in the desiccators over calcium chloride at temperature 37°C for 24 h. At room temperature, the tablets were weighed and exposed to 75% relative humidity (RH) for 2 weeks. By keeping saturated sodium chloride solution at the bottom of the desiccators for 3 days the required humidity was achieved. Pills were reweighed, and an increase in weight was reported in percentage.[28,29]

RESULTS

The standard curves of montelukast sodium in 0.5% SLS in purified water led to the curve equation, $y = 0.0649x + 0.0252$ and $R^2 = 0.997$.

The S_2, S_5, S_7 and S_2S_5, S_2S_7, S_5S_7 formulations were designed with super disintegrating agents [Table 3]. The E_8S_2, E_9S_2, E_8S_5, E_9S_5, E_8S_7, and E_9S_7 formulations were prepared with a combination of super disintegrating agents and effervescent bases [Table 4]. Results from the evaluation of the mixed powders including bulk density, tapped density, angle of repose, compressibility index, and Hausner's ratio are given in Tables 5. The results obtained from tablets evaluation including weight variation, friability, thickness, hardness, disintegration time, wetting time, content uniformity, and assay are presented in Table 6. An average weight of twenty tablets of all formulations with super disintegrating and combination super disintegrating with effervescent base was found in the range of 147–150 mg and 198.5–200.5 mg, respectively. The range of friability, thickness, and hardness of all the formulations was described in 0.27%–0.43%, 3.00–3.81 mm, and 33.7–37.1 N, respectively. Wetting time was found in the range of 31–50 s, which facilitate the faster dispersion in the mouth. Drug content of all formulations was found in the range of 96.28%–99.90%.

The *in vitro* disintegration time of the tablets was found in the range of 30–50 s in formulations with super disintegrating agents and 20–36 s in formulations with

a combination of super disintegrating and effervescent bases. *In vitro* dissolution studies of formulations at different time intervals are shown in Figure 1.

The results of taste evaluation are shown in Figure 2. According to the average assigned scores, the tutti-frutti flavor receives the highest score. Moisture uptake studies for formulations were performed at 75% RH, and the results were in the range of 0.2%–0.5%.

DISCUSSION

Montelukast sodium is a selective and orally active leukotriene receptor antagonist that used as an alternative to anti-inflammatory medications in the prevention and chronic treatment of asthma, alleviation of symptoms of seasonal allergies, and exercise-induced bronchospasm. This drug is available in the form of oral tablets and granules. Montelukast 5 mg chewable tablet is mostly used for prevention and treatment of asthma or allergic rhinitis, especially in children who have difficulty in swallowing or chewing conventional tablets.

The aim of this study was to design, formulate, and evaluate the physicochemical properties of montelukast ODTs to decrease disintegration time of tablet in the buccal and hence, to improve patient compliance.

Montelukast sodium standard curve in 0.5% SLS in purified water was plotted by UV spectrophotometry at λ_{max} of 346 nm. The results of this curve helped us for determination of the assay and content uniformity test.

The S_1–S_9 formulations were designed with a different amount of SSG (2%–8%), CCS (0.5%–5%), and CP (2%–5%). The final formulations were selected with the best disintegration time at a lower amount.[30] S_2S_5, S_2S_7, and S_5S_7 formulations were prepared with a combination of super disintegrating agents. The E_1–E_9 formulations were made up different effervescent components such as citric acid, tartaric acid, and sodium bicarbonate. According to the neutralization of alkali and acid and the ratios between them, concentration of each effervescent bases was determined,[31] but disintegration time of the tablets was found to be more than 60 s, so for decreasing

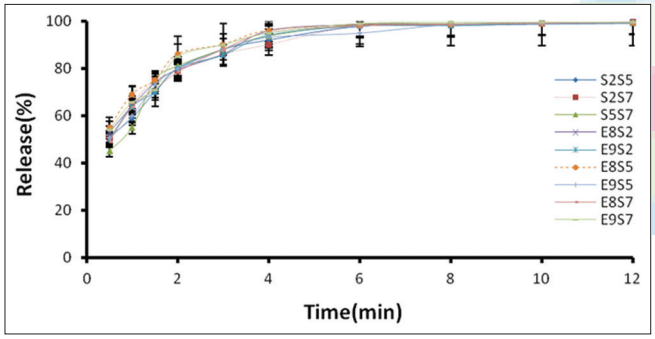

Figure 1: *In vitro* release of montelukast orally disintegrating tablets in 0.5% of SLS in purified water at 37°C (*n* = 3)

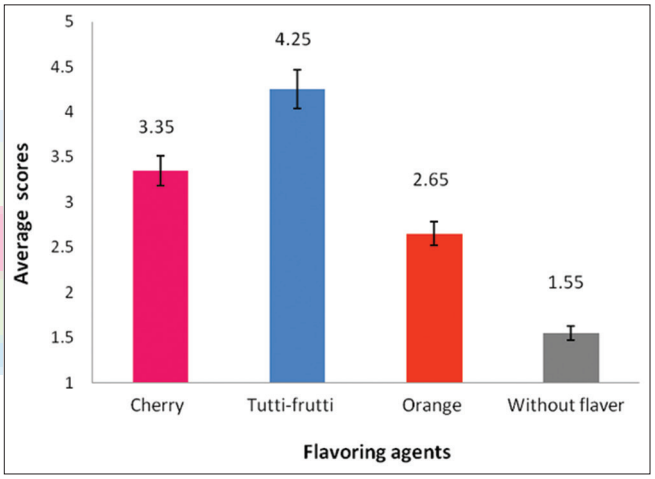

Figure 2: The results of taste evaluation of montelukast orally disintegrating tablets in panel tests by Latin-square method (*n* = 20)

Table 5: Physical characteristics evaluation of powder mixture (*n*=3)

Formulations	Physicochemical properties (mean±SD)				
	Tapped density (g/ml)	Bulk density (g/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose (θ)
S_2	0.64±0.04	0.49±0.03	23.43±0.03	1.30±0.01	34.14±0.71
S_5	0.64±0.03	0.50±0.02	21.87±0.02	1.28±0.02	33.93±0.50
S_7	0.65±0.01	0.50±0.01	23.07±0.01	1.30±0.02	34.48±0.56
S_2S_5	0.64±0.01	0.51±0.01	20.31±0.01	1.25±0.03	33.80±0.55
S_2S_7	0.63±0.02	0.49±0.01	22.22±0.02	1.28±0.01	33.60±0.58
S_5S_7	0.62±0.02	0.50±0.01	19.35±0.01	1.24±0.01	33.33±0.21
E_8S_2	0.63±0.02	0.53±0.01	15.87±0.02	1.18±0.02	32.93±0.47
E_9S_2	0.61±0.01	0.50±0.01	18.03±0.01	1.22±0.02	34.45±0.24
E_8S_5	0.63±0.01	0.52±0.02	17.46±0.01	1.21±0.01	33.82±0.53
E_9S_5	0.60±0.01	0.49±0.02	18.33±0.08	1.22±0.04	34.65±0.50
E_8S_7	0.63±0.02	0.50±0.01	19.04±0.01	1.26±0.01	34.49±0.58
E_9S_7	0.64±0.02	0.51±0.01	20.31±0.02	1.25±0.02	34.35±0.39

SD=Standard deviation

Table 6: Physicochemical evaluation of montelukast orally disintegrating tablets ($n=3$)

Physicochemical properties (mean±SD)	Formulations											
	S_2	S_5	S_7	S_2S_5	S_2S_7	S_5S_7	E_8S_2	E_9S_2	E_8S_5	E_9S_5	E_8S_7	E_9S_7
Weight variation (mg)	147.00±1.84	147.00±3.12	149.00±1.77	150.00±1.52	149.50±1.49	149.50±1.73	199.00±1.81	200.20±1.27	199.20±1.54	198.50±1.67	199.00±1.41	200.50±1.58
Hardness (*n*)	36.30±3.59	34.90±3.66	35.50±3.95	34.80±3.20	34.20±2.93	33.70±4.10	34.30±3.27	36.20±3.05	35.40±3.57	37.10±3.32	36.10±3.47	35.40±2.95
Thickness (mm)	3.01±0.03	3.02±0.04	3.00±0.00	3.01±0.03	3.01±0.03	0.37±0.18	3.80±0.00	3.81±0.01	3.81±0.02	3.80±0.03	3.80±0.06	3.81±0.03
Friability (%)	0.36±0.19	0.35±0.16	0.40±0.19	0.32±0.25	0.43±0.16	0.37±0.18	0.42±0.17	0.38±0.19	0.34±0.16	0.35±0.20	0.32±0.12	0.27±0.14
Disintegration time (s)	50±0.78	47±1.11	42±0.96	45±0.69	30±1.53	30±2.30	36±0.58	24±1.04	35±2.04	21±0.80	34±0.73	20±0.53
Wetting time (s)	50±0.81	44±0.73	38±0.54	49±1.45	35±1.71	34±1.24	47±2.00	33±1.35	43±1.22	31±0.83	37±1.73	31±1.56
Content uniformity (%)	96.28±2.16	96.85±1.96	97.49±1.86	99.45±0.76	97.69±1.64	98.00±1.76	98.78±1.65	97.90±1.09	97.85±2.21	99.90±1.61	98.14±1.59	98.90±1.43
Assay (mg)	4.86±0.35	4.95±0.15	4.92±0.21	4.97±0.14	4.95±0.19	5.01±0.14	4.89±0.21	4.81±0.32	4.92±0.19	5.01±0.16	4.97±0.11	5.02±0.13

SD=Standard deviation

disintegration time, E_8 and E_9 formulations that had the lowest disintegration time were combined with S_2, S_5, and S_7 formulations. E_8S_2, E_9S_2, E_8S_5, E_9S_5, E_8S_7, and E_9S_7 formulations were prepared with a combination of super disintegrant agents and effervescent bases.

The angle of repose is better obvious for flow property of all mixed powders. In this study, the angle of repose was in the range of 32.93–34.65. According to the USP specifications the flow properties of the powder blend, all formulations had medium to good flow. In the other study, on piroxicam ODTs angle of repose was in the range of 28.6–34.7[32] that confirms our results.

The hardness of ODTs is less than conventional tablets that in this study were observed in the range of 33.7–37.1 N, in other studies on ODTs of ondansetron, metoclopramide, and rizatriptan hardness of tablet were reported between 20 and 40 N[33-35] that showed the results were agreement with this study.

Friability values were <1% in all formulations (0.27%–0.43%). In another study, friability was in the range of 0.33%–0.66 and confirms our results.[32] The results of hardness and friability indicated that the tablets had suitable mechanical strength at the time of handling and transportation.

In the tablets, which their weight is between 130 and 324 mg, just two tablets can be exceed from ± 7.5% of the weight average (for tablets with 200 mg weight ± 15 mg and for tablets with 150 mg weight ± 11.25 mg)[23] that all tablets were in the range.

The content uniformity test was for the determination of fixed dose of medicine in individual tablets. Content uniformity of tablets was in acceptable 85%–115% limitation (96.28%–99.90%), which showed powders were uniformly mixed before tableting. All formulations had passed assay test successfully.

Disintegration time is the most important test in the preparation of ODTs. The shorter the disintegration time, the better it would be accepted by patients. Disintegration time of the tablets prepared with super disintegrating agents, effervescent bases, and combination of two was found to be in the range of 30–50, more than 60 and 20–36 s, respectively. The S_2S_7 and S_5S_7 between formulations prepared by super disintegrant agents and E_9S_7 between formulations combination of super disintegrant agents with effervescent bases were found to have shorter disintegration time. Swelling and effervescence are two mechanisms that was disintegrated tablets. In other studies, the disintegration time with super disintegrant agents has been reported between 9 and 72 s.[33-35]

The wetting time was in the range of 31–50 s. This time in most formulations was longer than disintegration time

since the tablet remained in plate level and was not soaked in water. In other studies, the wetting time has been reported between 9 and 75 s.[32-34] The difference in results can be related to kind of super disintegrant and ingredients and contact surface too. In similar study, the disintegration time was found to be in the range of 8–40 s, while the wetting time was found to be in the range of 13–40 s, also was observed that when CCS was used as disintegrant, the tablets disintegrated rapidly compared to CP and SSG,[36] but in this study, the tablets disintegrated rapidly with CP.

In vitro dissolution studies of formulations at different time intervals showed that drug release profiles of all formulations are the same and most formulations released 50% of the drug within 30 s. In other study, on ODTs of montelukast sodium with similar details of the dissolution test most formulations released 50% of the drug within 60 s.[18] This may be due to the difference in the method of preparation of tablets. According to the average assigned scores, the tutti-frutti flavor was chosen by volunteers. Moisture uptake studies for formulations were performed at 75% RH, and there was a slight moisture uptake observed in tablets. Hygroscopicity of most formulations leads to special packing requirements for ODTs.

CONCLUSIONS

The present work was aimed to formulate the ODT of montelukast sodium using super disintegrants, effervescent bases, and mixture of two. The results from *in vitro* disintegration time showed that the formulations prepared with super disintegrants and super disintegrants combined with effervescent bases were more beneficial than the formulations with effervescent bases alone. Formulation E_9S_7 showed minimum disintegration time compared to other formulations. S_7 containing CP showed minimum disintegration time between formulations with super disintegrants.

Acknowledgements
This study was supported by Isfahan University of Medical Sciences as a thesis research project numbered 393054.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Received: 22 Aug 15 **Accepted:** 06 Sep 16
Published: 26 Oct 16

REFERENCES

1. Lindgren S, Janzon L. Dysphagia: Prevalence of swallowing complaints and clinical finding. Med Clin North Am 1993;77:3-5.
2. FDA/CDER. Guidance for Industry: Orally Disintegrating Tablets. Rockville, MD: The United States Food and Drug Administration, Center for Drug Evaluation and Research; 2008.
3. Chang RK, Guo X, Burnside BA, Couch RA. Fast dissolving tablets. Pharm Technol 2000;24:52-9.
4. Parakh SR, Gothoskar AV. A review of mouth dissolving tablet technologies. Pharm Technol 2003;27:92-100.
5. Hanawa T, Watanabe A, Tsuchiya T, Ikoma R, Hidaka M, Sugihara M. New oral dosage form for elderly patients: Preparation and characterization of silk fibroin gel. Chem Pharm Bull (Tokyo) 1995;43:284-8.
6. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery-a review. Pharm Sci Technolo Today 2000;3:138-45.
7. Ashish P, Harsoliya MS, Pathan JK, Shruti S. A review- Formulation of mouth dissolving tablet. Int J Pharm Clin Sci 2011;1:1-8.
8. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. J Pharm Pharmacol 1998;50:375-82.
9. Liang AC, Chen LH. Fast-dissolving intraoral drug delivery systems. Expert Opin Ther Pat 2001;11:981-6.
10. Morita Y, Tsushima Y, Yasui M, Termoz R, Ajioka J, Takayama K. Evaluation of the disintegration time of rapidly disintegrating tablets via a novel method utilizing a CCD camera. Chem Pharm Bull (Tokyo) 2002;50:1181-6.
11. Schiermeier S, Schmidt PC. Fast dispersible ibuprofen tablets. Eur J Pharm Sci 2002;15:295-305.
12. Siewert M, Dressman J, Brown C, Shah VP. FIP/AAPS guidelines for dissolution/*in vitro* release testing of novel/special dosage forms. Dissolution Technol 2003;10:6-15.
13. Saroha K, Mathur P, Verma S, Syan N, Kumar A. Mouth dissolving tablets: An overview on future compaction in oral formulation technologies. Der Pharmacia Sinica 2010;1:179-87.
14. Vijaykumar G, Ajaykumar P, Satishkumar P, Karunasri S, Raghavender K, Priya P. Development and evaluation of fast-dissolving film of montelukast sodium. J Med Pharm Bio Sci 2011;1:6-12.
15. Raghavendra R, Upendra K. Formulation and design of fast dissolving tablet of felodipine using novel co-processed superdisintegrants. Int J Pharm Res Dev 2010;2:113-21.
16. Physician's Desk References. 64th ed., Montvale: NJ; Medical Economics Company, 2009. p. 2047-53.
17. Al Omari MM, Zoubi RM, Hasan EI, Khader TZ, Badwan AA. Effect of light and heat on the stability of montelukast in solution and in its solid state. J Pharm Biomed Anal 2007;45:465-71.
18. Mahesh E, Kumar GB, Ahmed MG, Kumar PK. Formulation and evaluation of montelukast sodium fast dissolving tablets. Asian J Biomed Pharm Sci 2012;2:75-82.
19. The United States Pharmacopeia, 31rd rev- The National Formulary 26th ed. Rockville, MD: United States Pharmacopeial Convention; 2008. p. 639-41, 676, 1269.
20. Nagar P, Singh K, Chauhan I, Verma M, Yasir M. Orally disintegrating tablets: Formulation, preparation techniques and evaluation. J Appl Pharm Sci 2011;1:35-45.
21. Patil MG, Kakade SM, Pathade SG. Formulation and evaluation of orally disintegrating tablet containing tramadol HCL by mass extrusion technique. J Appl Pharm Sci 2011;1:178-81.
22. Jeevanandham S, Dhachinamoorthi D, Chandrashekhar KB, Muthukumaran M, Sriram N. Formulation and evaluation of naproxen sodium orodispersible tablets – A sublimation technique. Asian J Pharm 2010; 4:48-51.
23. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea and Febiger; 1986. p. 334-5.
24. Saroha K, Kumar G, Paul Y. Formulation and evaluation of fast dissolving tablets of amoxicillin trihydrate using synthetic superdisintegrants. Int J Pharm Bio Sci 2013;4:254-62.
25. Khan S, Kataria P, Nakhat P, Yeole P. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS PharmSciTech 2007;8:127-133.
26. Devi NK, Rani AP, Mrudula BS. Formulation and evaluation of oral disintegrating tablets of montelukast sodium: Effect of functionality of superdisintegrants. J Pharm Res 2010;3:803-8.
27. Aslani A, Fattahi F. Formulation, characterization and physicochemical evaluation of potassium citrate effervescent tablets. Adv Pharm Bull 2013;3:217-25.
28. Thakur RR, Kashi M. An unlimited scope for novel formulations as orally

disintegrating systems: Present and future prospects. J Appl Pharm Sci 2011;1:13-9.
29. Kolhe S, More D. Updated review on orally disintergarting tablets: Advancement in current trends. Asian J Pharm Tech 2013;3:45-51.
30. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 7th ed. London: Pharmaceutical Press; 2012. p. 224, 227, 757.
31. Aslani A, Jahangiri H. Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. Adv Pharm Bull 2013;3:315-22.
32. Bhupendra GP, Bhaskar P. Formulation, evaluation and optimization of orally disintegrating tablet of piroxicam. Int J Pharm Tech Res 2010;2:1893-9.
33. Bansal N, Sharma G. Formulation and evaluation of orally disintegrating tablets of ondansetron hydrochloride using natural superdisintegrants. Int J Pharm Tech Res 2011;3:1616-21.
34. Nagendrakumar D, Keshavshetti GG, Pratibha. Design and evaluation of fast dissolving tablets of metoclopramide hydrochloride using synthetic and natural superdisintegrants. Unique J Pharm Biol Sci 2014;2:16-24.
35. Parthiban KG, Kumar MP. Formulation and evaluation of oral dispersible tablets of rizatriptan benzoate. Int J Curr Pharm Res 2013;5:31-5.
36. Sri KV, Raj GB, Ravishanker D, Kumar CA. Preparation and evaluation of montelukast oral dispersible tablets by direct compression method. Int Res J Pharm 2012;3:315-8.