World Journal of Pharmaceutical research

Volume 2, Issue 6, 2662-2673. Research Article ISSN 2277 – 7105

FORMULATION, CHARACTERIZATION AND EVALUATION PARAMETERS OF FAST DISSOLVING TABLETS OF ONDANSETRON HCL

Y.Ganesh Kumar[1]*, M.Sindhu Reddy[2], P.Nithin Kumar[3], SK.Nayab Rasool[4], K.Srinivasulu[4].

[1]Research Scholar, Faculty of Pharmaceutical Sciences, JNTU Hyderabad, A.P, India

[2]T.John College of Pharmacy, Bangalore, K.A, India.

[3]Vikas College of Pharmacy, Shameerpet, Jangaon, Warangal, A.P, India.

[4]Srivani School of Pharmacy, Chevuturu, Vijayawada, Krishna.Dist, A.P, India.

Article Received on
18 August 2013,

Revised on 25 Sept. 2013,
Accepted on 30 October 2013

***Correspondence for Author:**

Y.Ganesh Kumar
Research Scholar, Faculty of Pharmaceutical Sciences,
JNTU Hyderabad, A.P, India
ganesh.yed@gmail.com

ABSTRACT

Ondansetron is a Serotonin 5-HT_3 Receptor antagonist used mainly as an Antiemetic Drug. It affects both peripheral and central nerves. Ondansetron reduces the activity of the vagus nerve, which deactivates the vomiting center in the medulla oblongata, and also blocks serotonin receptors in the chemoreceptor trigger zone. Ondansetron is well absorbed after oral administration and undergoes limited first-pass metabolism. Oral bioavailability of 60% due to hepatic first pass metabolism and has a short half-life of 5.7 hours. And Plasma Protein binding is a 70-76%.The present study was carried out to formulate and evaluate fast dissolving tablets of Ondansetron hydrochloride for Oral administration. The prepared powder blends were then compressed into tablets using the necessary Superdisintegrants and Excipients. The tablets were evaluated for Weight variation, thickness, hardness, friability, Drug Content and Disintegrating Time (Sec) were subjected to a 9 minutes *in vitro* drug release studies (USP dissolution rate test apparatus II, 50 rpm, 37^0C ±0.5^0C) using phosphate buffer, pH 6.8 as a dissolution medium (900ml). The amount of Ondansetron released from the tablet formulations at different time intervals was estimated using a UV spectroscopy method. The formulations that showed a considerable retardation of the drug release are considered promising. Among the Eight formulations, F5 formulation containing Drug to Sodium Starch

Glycollate (SSG) in ratio 1:1 is optimized based on its ability to till 9 minutes of invitro dissolution time, and its % Cumulative Drug Release is 98.27%.

Key Words: Serotonin 5-HT_3 Receptor antagonist, Chemoreceptor trigger zone, Direct Compression, Superdisintegrants.

INTRODUCTION

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance. The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance. Tablets and capsules are the most popular dosage forms. Pharmaceutical technologists have put in their best efforts to develop a Fast dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few sec without the need of drinking water or chewing[1,2,3].

MATERIALS AND METHODS

Materials

Ondansetron was a gift sample from MSN Laboratories Ltd, Hyderabad, Andhra Pradesh., Microcrystalline Cellulose, Aerosil, Magnesium Stearate, Croscarmellose Sodium was used and supplied by Bright Labs, Hyderabad, Mannitol, Sodium Starch Glycolate, Crospovidone was supplied by yarrow chem. products, Mumbai, India.

METHODOLOGY

Formulation of Ondansetron Tablet by Direct Compression

Composition of preliminary trials for Ondansetron Tablets by direct compression. All the ingredients were weighed. Required quantity of drug and Excipients mixed thoroughly in a Polybag. The blend is compressed using rotary tablet machine-12 station with 8mm flat punch, B tooling. Each tablet contains 100 mg Ondansetron and other pharmaceutical ingredients.

Table 1: Formulation chart of Ondansetron

INGRADIENTS	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Ondansetron	4	4	4	4	4	4	4	4
Croscarmellose sodium	2	4	6	-----	-----	-----	-----	-----
Sodium starch glycolate	-----	-----	-----	2	4	6	-----	-----
Crospovidone	-----	-----	-----	-----	-----	-----	2	4
Aerosil	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2
Micro crystalline Cellulose	65	65	65	65	65	65	65	65
Total	75	75	75	75	75	75	75	75

EVALUATION PARAMETERS

Precompression parameters

1. Bulk Density (D_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

2. Tapped Density (D_t)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where, M is the mass of powder

V_t is the tapped volume of the powder.

3. Angle of Repose (Θ)

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane

tan (Θ) = h / r

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particles slip and roll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property[4,5,6].

Table 2: Angle of Repose as an Indication of Powder Flow Properties

S.No	Angle Of Repose	Type Of Flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very Poor

4. Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is give by,

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where, D_t is the tapped density of the powder and

D_b is the bulk density of the powder.

Table 3: Relationship between % compressibility and flow ability

S.No.	% Compressibility	Flow ability
1	5-12	Excellent
2	12-16	Good
3	18-21	Fair Passable
4	23-35	Poor
5	33-38	Very Poor
6	<40	Very Very Poor

5. Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following Formula:

$$\text{Hausner Ratio} = \frac{D_t}{D_b}$$

Where, D_t is the tapped density, D_b is the bulk density.

Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Post compression parameters

1. Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation.

Average Weight of Tablets	%Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Table 4: Weight Variation Specification as per IP

2. Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

3. Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper.

4. Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at the height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

5. Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipients. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

dl/dt = r¡cosϴ/(4hl)

It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place. A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37^{o}C.Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

6. *In-Vitro* drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile.

Dissolution test

USP II Paddle apparatus was used and paddle was allowed to rotate at 50 rpm, 6.8 Phosphate buffer (900 ml) was used as a dissolution medium[7-14].

RESULTS AND DISCUSSION

Standardization of Ondansetron by UV/VIS Spectrophotometer

Standard calibration of Ondansetron in 6.8 Phosphate buffer

100mg of Ondansetron was accurately weighed and dissolved in100ml of 6.8 phosphate buffer to obtain a concentration of 1000µg/ml. From the above 10ml was withdrawn and diluted to 100ml to obtain a concentration of 100µg/ml. From this stock solution aliquots of 0.5ml, 1ml, 1.5ml, 2ml and 2.5ml were diluted in 10ml volumetric flask with phosphate buffer to give concentrations in range of 5µg/ml to 25µg/ml respectively, absorbance was measured at 230 nm.

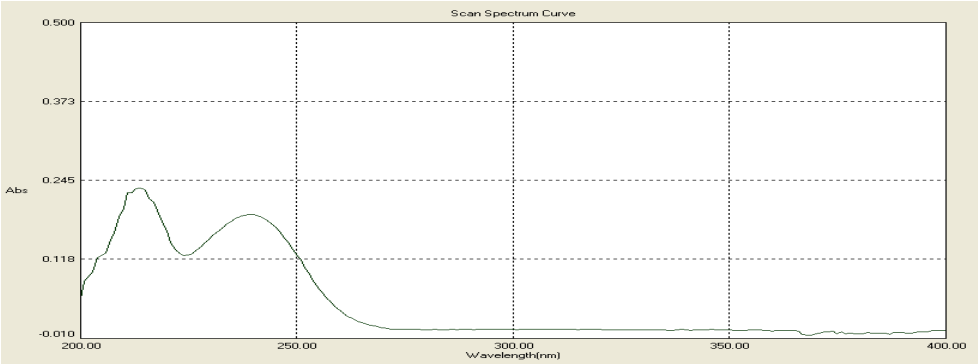

Fig 1: Standard Calibration curve of Ondansetron

Table 5: Standard graph of Ondansetron in 6.8 Phosphate buffer

Concentration	Absorbance
0	0
2	0.241
4	0.542
6	0.775
8	0.998

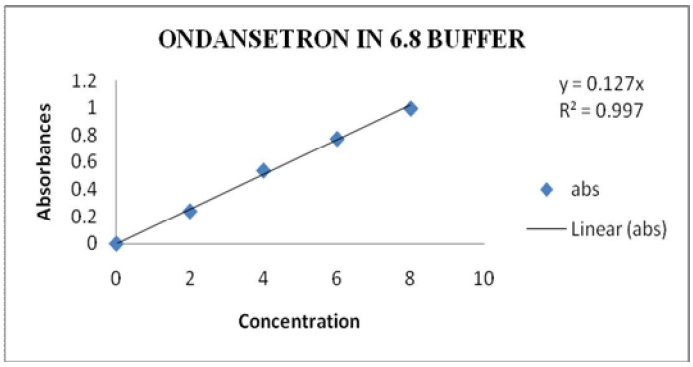

Table 5.1: Concentration and absorbance obtained for calibration curve of Ondansetron in 6 .8 Phosphate buffer

Pre Compression parameters

Table 6: Pre Compression parameter of Ondansetron tablets

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle Of Repose
F_1	0.45	0.55	18.18	1.22	27.91
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	13.79	1.16	29.34

F_4	0.46	0.55	16.36	1.19	26.71
F_5	0.50	0.58	13.79	1.16	29.34
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.44	0.57	15.75	1.18	27.67
F_8	0.49	0.59	14.49	1.17	28.9

Post Compression parameters

Table7: Post Compression parameter of Ondansetron tablets

Formulations	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Wetting time (sec)
F_1	75	2.33	2.59	20.33	0.43	19.33
F_2	74.5	2.66	2.64	22.66	0.34	18.00
F_3	76.1	2.66	2.59	30.33	0.49	24.66
F_4	75.2	2.00	2.58	33.10	0.47	14.33
F_5	74.8	2.66	2.59	19.00	0.49	24.66
F_6	74.5	2.66	2.64	22.66	0.34	18.00
F_7	75.1	2.41	2.13	26.25	0.32	25.23
F_8	75	2.12	1.98	24.56	0.41	26.75

Dissolution profile and percentage drug release of formulations (F_1-F_8)

Table 8: Dissolution profile and percentage of drug release of all formulations

S.No	Time (Mins)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	0	0	0	0	0	**0**	0	0	0
2	1	20.38	28.95	17.38	23.56	**28.59**	21.54	19.69	26.18
3	2	35.19	41.75	31.48	37.54	**43.64**	36.73	31.82	41.27
4	3	41.95	50.17	43.72	49.45	**59.38**	48.76	49.17	51.62
5	5	52.64	62.83	60.59	69.23	**72.71**	59.29	61.97	64.75
6	7	69.32	76.40	80.34	78.29	**85.27**	73.28	74.27	76.84
7	9	82.65	92.51	93.10	90.18	**98.27**	87.17	91.43	94.35

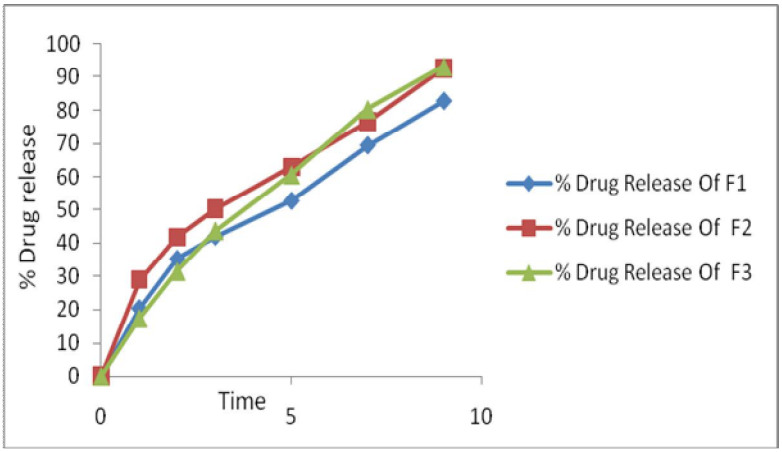

Fig 2: % Drug release of formulations(F1-F3)

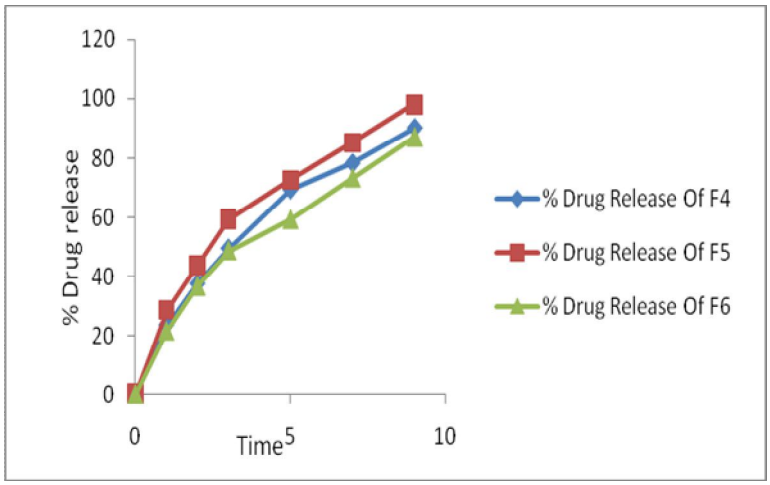

Fig 3: % Drug release of formulations(F4-F6)

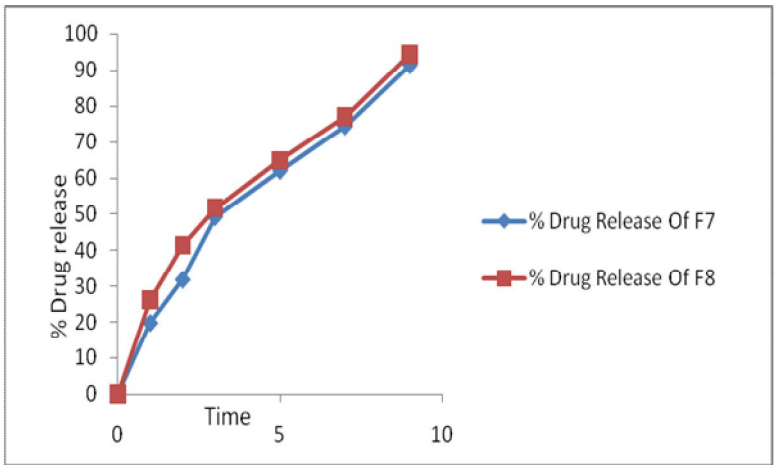

Fig 4: % Drug release of formulations(F7-F8)

Drug: Excipient Compatibility studies- FTIR

Drug-Excipient compatibility studies by FTIR revealed no interaction between drug and the polymers used in the formulation thus showing compatibility.

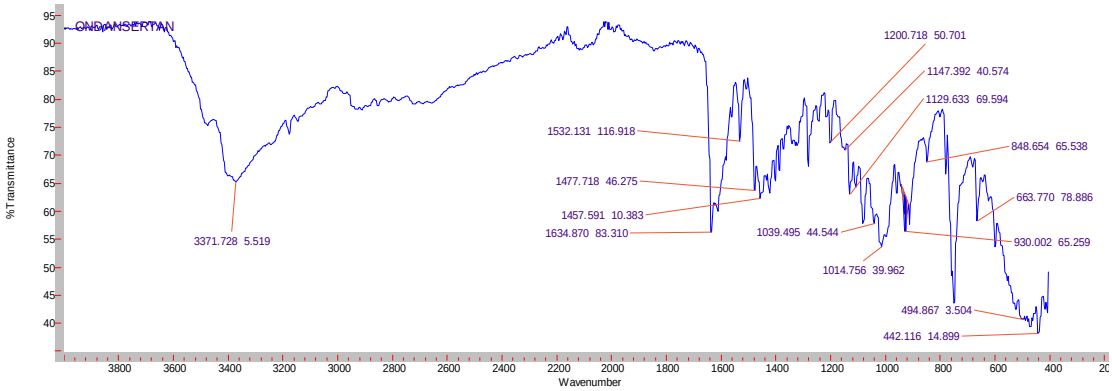

Fig 5: FTIR Spectrum of Ondansetron Pure Drug

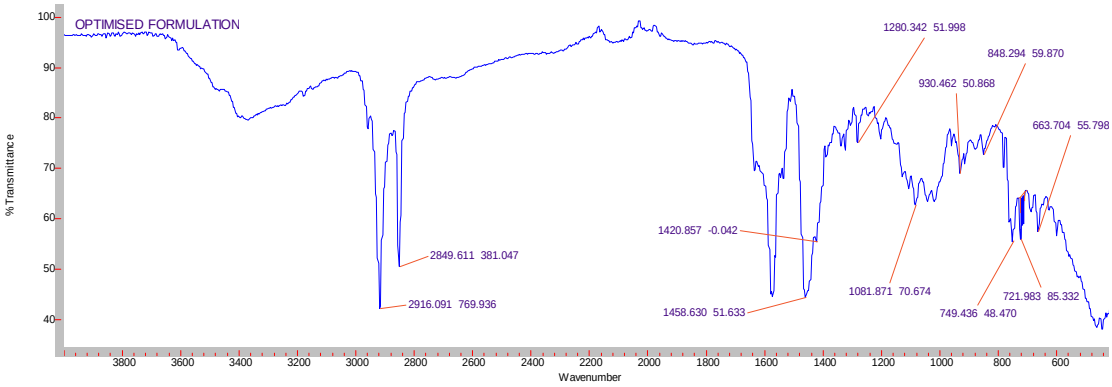

Fig 6: FTIR Spectrum of Optimized Formulation

CONCLUSION

- In the present work, an attempt has been made to develop fast disintegrating tablets of Ondensetron.The IR spectra revealed that; there was no interaction between Superdisintegrants and drug. All Super disintegrants used were compatible with drug.
- The result of physical parameter of preliminary trials by direct compression showed good flow property. Amongst the various combinations of diluents and disintegrants used in the study, tablets that were formulated (Direct compression) using Crospovidone, Croscarmellose sodium and Sodium starch glycolate exhibited quicker disintegration of tablets than compared to those other combination of disintegrants in different concentration. The effectiveness of Superdisintegrants was in order of SSG>CP>CCS.
- Finally, the tablets were evaluated for *in vitro* dissolution studies in Phosphate buffer (P^H-6.8) and the results were shown in the Formulations F1, F2, F6, F8, showed more than 90% of drug release within 30 min, whereas in formulation F2, F3, F4, F5, F7 and F8 showed 75-90% of drug release within 30 min. This result exhibit a direct relationship between concentration of superdisintegrants and drug release. Among the various

formulations tablets of batch F5 prepared with sodium starch glycolate showed 98.27release of drug within 9 min.

- Formulation **F5** was the optimized formulation having least disintegration time as well as other parameters was in acceptable range. Based on the optimization results it is concluded that the objective of formulating Orally Disintegrating Tablets containing Ondansetron has been achieved with success.
- The Pre compression parameters like Bulk density, Tapped density, Carr's index and Angle of repose were determined. All the 8 formulations showed acceptable flow properties.
- The Post compression parameters of the tablet like Hardness, Thickness, Friability and Weight variation, Disintegration time, Wetting time, and Invitro release were carried out and the values were found to be within IP limits.

ACKNOWLEDGEMENT

The authors are thankful for the management of MSN Laboratories Ltd Hyderabad, Bright Labs Hyderabad, Andhra Pradesh, India and Yarrow Chem Products, Mumbai, India. For the gift samples of drug and polymers used in the work.

REFERENCES

1. Chein YW. Oral Drug Delivery and Delivery Systems. 2nd Ed. New York: Marcel Dekker; 1992.
2. Debjit B, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. J Chem Pharm Res. 2009; 1(1): 163-77.
3. Kaur T, Bhawandeep G, Sandeep K, Gupta GD. Mouth dissolving tablets: a novel approach to drug delivery. Int J Curr Pharm Res. 2011; 3(1): 1-7.
4. Augsburger LL, Stephen WH. Orally disintegrating tablets. Pharmaceutical dosage forms: tablets. Infroma Healthcare Publication, 3rd ed., 2; 293-312.
5. Mohanachandran PS, Krishnamohan PR, Fels S, Bini KB, Beenu B, Shalina KK. Formulation and evaluation of mouth dispersible tablets of amlodipine besylate. Int J App Pharm. 2010 Apr; 2(3): 1-6.
6. Nitin S, Sanjula B, Alka A, Javed A. Fast-dissolving intra-oral drug delivery systems. Expert Opin Ther Patents. 2008; 18(7): 769-81.
7. Bipin P, Patel JK, Ganesh R, Rashmin T. Formulation and evaluation of mouth dissolving tablets of cinnarizine. J Pharm Res. 2009 Mar; 3(2): 510-13.

8. Mutasem MR, Estelle RS, Keith JS. Fast-disintegrating sublingual epinephrine tablets: effect of tablet dimensions on tablet characteristics. Drug Dev Ind Pharm. 2007; 33: 523-30.
9. Jinichi F, Etsue Y, Yasuo Y, Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. Int J Pharm. 2006; 310: 101-09.
10. Sameer GL, Yi-ying Y, Ajay KB. Effects of disintegration-promoting agent, lubricants and moisture treatment on optimized fast disintegrating tablets. Int J Pharm. 2009; 365: 4-11.
11. Shery J, Arun S, Anroop N. Preparation and evaluation of fast-disintegrating effervescent tablets of glibenclamide. Drug Dev Ind Pharm. 2009; 35: 321-28.
12. Simone S, Peter CS. Fast dispersible ibuprofen tablets. Eur J Pharmaceut Sci. 2002 Feb 1; 15: 295–305.
13. Deshika R, Viness P, Yahya EC, Lisa CT. Rapidly disintegrating oramucosal drug delivery technologies. Pharm Dev Tech. 2009; 14(6): 588-601.
14. Rahul C, Zahra H, Farhan A, Alan MS, Afzal RM. The role of formulation excipients in the development of lyophilized fast-disintegrating tablets. Eur J Pharm Biopharm. 2009; 72: 119-29.