

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF A MODEL ANTI-HYPERTENSIVE DRUG

S. P. HIREMATH*, CHIDAMBAR MAKANAPUR

Department of Pharmaceutics, KLE University's College of Pharmacy, Hubli 580031, Karnataka, India
Email: hiremathsp2005@gmail.com

Received: 06 Apr 2017 Revised and Accepted: 21 Sep 2017

ABSTRACT

Objective: The rationale of the current work was to formulate and evaluate orodispersible tablets by direct compression technique with a vision to augment patient compliance and rapid onset of action.

Methods: Nine orodispersible formulations of propranolol were formulated by direct compression method using sodium starch glycolate, crospovidone and croscarmellose sodium as the super disintegrants. The prepared formulations were evaluated for wetting time, drug content, *in vitro* disintegration time, dispersion time, dissolution time and also projected to kinetic treatment to know the pattern of drug release. Further, the discovered promising formulation was subjected to stability studies.

Results: Based on the results obtained, formulation F9 containing 6 mg of croscarmellose sodium exhibited good wetting time, dispersion time, and disintegration time and drug release compared to orodispersible tablets prepared with other super disintegrants. The stability studies piloted as per International Conference on Harmonisation guidelines on the promising formulation F9 disclosed no significant changes in the colour (white), drug content (94.87±0.141 mg), hardness (2.93±0.18 kg/cm²), disintegration time (17.11±0.089 s), and drug release after 4 w. After 60 s, the percentage drug release of F9 was found to be 98.52 % and 96.30 % after 1 and 4 w, respectively.

Conclusion: Orodispersible tablets of propranolol hydrochloride were formulated successfully by employing direct compression technique. From the investigation, it can be reasonably concluded that F9 batch orodispersible tablets of propranolol with 6 mg of crospovidone exhibited maximum cumulative drug release in 60 s.

Keywords: Propranolol, Orodispersible tablets, Direct compression technique, Superdisintegrants

© 2017 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open-access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)
DOI: <http://dx.doi.org/10.22159/ijpps.2017v9i11.18967>

INTRODUCTION

Oral dosage forms, both the solids and liquids, have been the most extensively accepted routes of drug delivery for decades now. It is widely accepted because of its advantages such as self-medication, ease of administration, pain avoidance, and patient compliance [1, 2]. However, the evident shortcomings of this route are difficulty in swallowing and patient noncompliance, especially in paediatric, geriatric, nauseated, and mentally ill patients [3, 4]. All these restraints could be resolved by one of the recent pioneering advances in novel drug delivery system (NDDS)—by orally disintegrating tablets (ODT).

ODT technology has been recently approved by the United States Pharmacopoeia (USP) and Centre for Drug Evaluation and Research (CDER) [4]. As per United States Food and Drug Administration (USFDA), ODT is a solid dosage form comprising medicinal constituent, which instantaneously dissipates within seconds into the saliva when kept on the tongue [5]. The drug will be absorbed as the saliva gradually passes down from the mouth, pharynx, oesophagus, and stomach [6].

The principal benefits of ODT include meliorated patient compliance, improved bioavailability, rapid onset of action, pain avoidance, consumption without water, pregastric absorption, versatility, and economical [7-9]. Pregastric absorption is the major capital advantage of the ODTs, which avoids hepatic first-pass metabolism of the drugs [10].

Propranolol, a nonselective beta blocker, is used to treat major disorders such as acute myocardial infarction, angina pectoris, arrhythmias, hypertension, hyperthyroidism, hypertensive emergencies, menopause, pheochromocytoma, migraine, and anxiety [11]. Propranolol hydrochloride competes with the sympathomimetic neurotransmitters and prevents the binding of catecholamines at beta (1)-adrenergic receptors present in the

heart. This results in a decrease of diastolic and systolic and blood pressure, cardiac output, and reflex orthostatic hypotension [11].

The present work was attempted to develop an orodispersible antihypertensive tablet, which dissipates instantaneously in the oral cavity within few seconds without the aid of water. This will enhance the dissolution rate and bioavailability along with the rapid onset of pharmacological action. In the current development, the ODTs of propranolol were formulated by direct compression technique using crospovidone, sodium starch glycolate and croscarmellose sodium, as the super disintegrants to augment patient compliance and rapid onset of action.

MATERIALS AND METHODS

The active pharmaceutical ingredient—propranolol hydrochloride was procured from Micro labs, Bengaluru. The other excipients such as magnesium stearate, purified talc, and mannitol were procured from SD Fine Chemicals (Mumbai). Sodium starch glycolate and croscarmellose sodium were purchased from Maruthi Chemicals Ltd. (Ahmedabad), and crospovidone was purchased from Kawaral excipients (P) Ltd (Chennai). Microcrystalline cellulose pH 102 was purchased from Elegant pharmaceuticals (Hubli). Aspartame was purchased from Nutra Sweet Company.

Formulation of orodispersible tablets

Orodispersible tablets of propranolol were formulated by the direct compression technique. The details of composition for the formulations are mentioned in table 1. All the ingredients except talc and magnesium stearate were weighed accordingly and mixed thoroughly to ensure proper mixing of drug with the super disintegrants. The mixture was sifted through a sieve no. 40 and then blended with talc and magnesium stearate. Finally, the blended mixture was subjected to compression using rimek tablet punching machine using 6.5 mm flat and circular punch.

Table 1: The quantity of ingredients for the designed formulations of propranolol orodispersible tablets by direct compression technique

Ingredients	Composition (mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Propranolol HCl	40	40	40	40	40	40	40	40	40
Sodium starch glycolate	3.6	4.8	6	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	3.6	4.8	6	-	-	-
Crospovidone	-	-	-	-	-	-	3.6	4.8	6
Mannitol	24	24	24	24	24	24	24	24	24
Microcrystalline cellulose pH102	47.6	46.4	45.2	47.6	46.4	45.2	47.6	46.4	45.2
Aspartame	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Purified talc	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Magnesium stearate	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4
Total weight	120	120	120	120	120	120	120	120	120

HCl: Hydrochloride

Evaluation of orodispersible tablets

The formulated ODTs were evaluated for physiochemical parameters such as general appearance, weight variation test, uniformity of thickness, friability test, hardness test, and drug content uniformity. The other key parameters which were especially evaluated are following:

Drug content

Five tablets from each formulation were randomly selected, accurately weighed, and average weight per tablet was calculated. Each tablet was pulverized to a very fine powder and a known amount of drug that is equivalent to 40 mg of propranolol hydrochloride was transferred into a 100-ml volumetric flask. Phosphate buffer (6.8 pH) was used to dissolve the drug and solution was made up to the mark. The solution was strained and from which 1 ml was withdrawn into a 10-ml volumetric flask and diluted with buffer. The resultant solution was determined spectrophotometrically at 290 nm [12].

Wetting time

Wetting time was performed to determine the disintegration properties of the tablet. Lower wetting time indicates a faster disintegration of the tablet. A section of tissue paper of 10.75 cm diameter was folded twice and placed in a petri dish containing 10 ml of water. An ODT was placed carefully on the surface of butter paper and the time consumed for complete wetting was taken as a wetting time [13].

In vitro dispersion time

The dispersion time was determined by dropping an ODT in a measuring cylinder having 50 ml of simulated saliva fluid of pH of 6.8. Three tablets from each batch were selected arbitrarily and *in vitro* dispersion time was measured [14].

In vitro disintegration time

The disintegration time of ODT was determined by disintegration apparatus as per Indian Pharmacopoeia (IP) specifications. Each ODT was placed in six tubes of the basket and a disc was placed in all six tubes to prevent the floating of tablets. The simulated saliva, fluid of pH 6.8, maintained at 37 (\pm 2) °C, was used as an immersion liquid. The whole assembly placed in immersion liquid was raised and lowered at 30 cycles/min frequency. The time taken for the complete disintegration of ODT with no residue remaining in the apparatus was recorded [15, 16].

In vitro dissolution studies

The dissolution studies of ODT were accomplished using United States Pharmacopoeia (USP) XXIV type II paddle type dissolution apparatus at 50 rpm. The release profile of the drugs was studied in 900 ml of 0.1 N hydrochloric acid buffer of pH 1.2 or phosphate buffer of pH 6.8 maintained at temperature 37 \pm 0.5 °C. For every 30 s, 2 ml of the aliquots was withdrawn, filtered, diluted suitably; and the amount of the drug release was determined spectrophotometrically at 290 nm. After the each withdrawal, the same volume replaced into the apparatus to keep the sink conditions [17-20].

Release kinetics

The cumulative drug release data obtained from formulations were subjected to different kinetic models such as zero-order kinetics, first-order kinetics, Higuchi model, and Korsmeyer-peppas release model [21-23].

Zero-order kinetic model: $C = K_0 t$

Where, K_0 = zero-order rate constant (concentration/time)

t = time

First-order kinetic model: $\log C = \log C_0 - K_1 t/2.303$

Where C_0 =initial drug concentration and K_1 is first-order constant

Higuchi model: $f_t = K_H t^{1/2}$

Where, f_t =amount of drug released in time t

K_H =Higuchi dissociation constant

Korsmeyer-peppas model: $M_t/M_\infty = Kt^n$

Where M_t/M_∞ = fraction of drug release

K =drug release constant

t =release time

n =diffusion coefficient, which characterizes the drug release, depends on the shape of the matrix dosage form.

Hixson-Crowell model: $W_0^{1/3} - W_t^{1/3} = kt$

Where, W_0 =initial amount of drug in the formulation

W_t =amount of drug remained in the formulation after time ' t '

K =constant incorporating surface-volume relation

Stability studies

The stability studies for the promising formulation were executed based on International Conference on Harmonisation (ICH) guidelines. The promising ODT was subjected to 40 \pm 2°C and 75 \pm 5% relative humidity for 30 d. After the specific period is finished, the ODT was once again subjected to all the tests to determine any variance in colour, hardness, drug content uniformity, % cumulative drug release (CDR), *in vitro* disintegration time [8].

RESULTS AND DISCUSSION

Oral drug delivery, one of the most frontier zones of drug delivery system, has a major benefit of patient compliance. The ODTs belong to the category of oral drug delivery disintegrates and release the medicament rapidly in the oral cavity. The release rate of the drug chiefly depends upon the type and concentration of the super disintegrants, which swell and lead to rapid wicking or bursting of the drug.

In the current investigation, an attempt has been made to formulate and evaluate ODTs of propranolol hydrochloride used in the

management of hypertension. The ODTs were formulated by direct compression technique using super disintegrants—sodium starch glycolate, croscarmellose sodium, crospovidone, and other additives.

Wetting time

The tablet, when placed in the saliva, mimics the action of it and lead to water uptake and subsequent wetting of the tablet. The wetting time depends on the inner structure of ODT. Since the dissolution process of ODT depends upon the wetting time, followed by disintegration time it could be expected that wetting time might be the cause of disintegration [24]. The wetting time of the formulations was observed to be in the range of 28.71 ± 0.986 to 76.47 ± 2.093 s. It was observed that wetting time was very rapid in crospovidone followed by croscarmellose sodium and the sodium starch glycolate (table 2).

Drug content

The drug content uniformity was executed for all the nine formulations and results are tabulated in table 2. The drug content of the ODTs was found to be in the range of 93.87 ± 0.015 to 99.87 ± 0.013 mg. The results obtained were within the Pharmacopeial limits and indicated uniformity of mixing. The *in-vitro* release studies showed that the cumulative percentage drug released by each ODT was based on the average drug content of the tablet [25].

In vitro dispersion time

The dispersion time is a parameter, which was executed to determine the time period taken for the ODT to undergo complete dispersion. The dispersion time for the nine formulations was varied within the range of 25.09 ± 1.313 to 63.88 ± 1.186 s. Among these, formulation F9 containing 6 mg crospovidone exhibited faster dispersion. The quicker disintegration of crospovidone ODTs may be due to its fast capillary activity [26]. The corresponding results were shown in table 2. Among all formulations, *in vitro* dispersion was fast in crospovidone followed by croscarmellose sodium and Sodium starch glycolate [14].

In vitro disintegration time

The disintegration time of the formulations was varied from 18.65 ± 0.680 to 55.13 ± 1.160 s. The formulations with crospovidone exhibited rapid drug disintegration pursued by croscarmellose sodium and sodium starch glycolate. The rapid disintegration is due to prompt uptake of water from dissolution medium, bulging, and burst effect. Moreover, it was noted that as the concentration of super disintegrant increases the time consumed for disintegration was decreased [14]. The corresponding disintegration times for each formulation at predetermined times were shown in table 2.

Table 2: Drug content uniformity, *in vitro* disintegration time, dispersion time, and wetting time of formulations of F1-F9

Formulation code	Drug content (mg) uniformity	<i>In vitro</i> dispersion time in seconds	<i>In vitro</i> disintegration time in seconds	Wetting time in seconds
F1	95.37±0.088	63.88±1.186	55.13±1.160	76.47±2.093
F2	96.87±0.125	56.82±0.740	45.50±1.523	67.91±1.193
F3	98.87±1.016	48.26±0.890	33.62±1.670	53.59±2.823
F4	99.37±0.013	47.15±1.770	36.25±1.280	51.80±1.370
F5	93.87±0.015	41.86±1.040	31.94±1.110	48.12±1.260
F6	98.37±0.054	37.61±0.753	25.09±1.296	44.01±1.870
F7	98.87±0.026	38.20 ± 1.010	32.17±1.144	46.40±1.080
F8	99.87±0.013	32.07 ± 0.970	24.16±1.086	44.37±0.710
F9	97.37±0.032	25.09 ± 1.313	18.65±0.680	28.71±0.986

Data expressed in mean±SD, (n=3)

In vitro dissolution studies

Superdisintegrants accelerates the disintegration of the tablet by their ability to imbibe large amounts of water when exposed to an aqueous environment. The absorption of water consequences in breaking of tablets and consequently faster disintegration. This disintegration is stated to have an effect on dissolution characteristics as well. Formulated ODTs gets dispersed in the mouth rapidly and releases the drug early as compared to its prepared conventional tablets [27]. The data obtained from the dissolution studies disclosed that as the concentration of super

disintegrant increases the percentage of drug release was also increases. The rapid breakdown and absorption of the particles in the dissolution medium were mainly due to the concentration of super disintegrant. Among all formulations, F9 formulated with 6 mg of crospovidone exhibited 98.96% cumulative drug release in 60s.

In addition, the drug release profile from all formulations was observed to be concentration dependent [27]. Including this, formulation F9 also showed short wetting time, good drug content, and fast disintegration. The corresponding drug release pattern of each formulation at predetermined intervals is shown in table 3 and 4.

Table 3: *In vitro* dissolution profile of the formulations F4-F9

Time (s)	% CDR			
	F1	F2	F3	F4
0	0	0	0	0
30	38.62±0.982	49.69±0.922	51.02±0.912	43.49±0.988
60	43.09±0.992	64.38±0.978	65.71±0.943	65.26±0.962
90	63.05±0.986	71.47±0.988	84.33±0.985	83.02±0.977
120	70.14±0.896	83.05±0.963	91.87±0.923	93.20±0.981
150	82.56±0.943	90.98±0.956	-	-
180	89.21±0.967	-	-	-

CDR: Cumulative drug release; F: Formulation; Data expressed in mean±SD, (n=3)

Release kinetics

The kinetic release data attained for the promising formulation was projected to kinetic treatment to determine the drug release order.

The data obtained from different models—zero-order kinetics, first-order kinetics, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas models disclosed that the promising formulation exhibited Korsmeyer-Peppas as the best fitting model (table 4).

Table 4: *In vitro* dissolution profile of the formulations F5-F9

Time (s)	% CDR				
	F5	F6	F7	F8	F9
0	0	0	0	0	0
30	53.23±0.912	55.01±0.910	56.33±0.933	66.08±0.917	88.28±0.914
60	74.13±0.895	75.02±0.897	76.79±0.966	87.43±0.893	98.96±0.925
90	94.09±0.911	94.97±0.912	87.88±0.918	97.19±0.931	-
120	-	-	95.86±0.898	-	-
150	-	-	-	-	-
180	-	-	-	-	-

CDR: Cumulative drug release; F: Formulation; Data expressed in mean±SD, (n=3)

Table 4: Curve fitting data of the release rate profile of formulations F1-F9

Formulation	Zero-order		First order		Higuchi		Korsmeyer-peppas			Hixon-crowell		Best fitting model
	R	k	R	k	R	k	R	k	n	R	k	
F1	0.755	0.024	0.541	-0.0001	0.934	0.061	0.974	0.146	0.146	0.622	-0.0002	Peppas
F2	0.777	0.031	0.744	-0.0000	0.923	0.058	0.982	0.157	0.131	0.544	-0.0003	Peppas
F3	0.840	0.054	0.766	-0.0005	0.936	0.095	0.967	0.121	0.253	0.659	-0.0003	Peppas
F4	0.830	0.034	0.814	-0.0003	0.978	0.148	0.999	0.162	0.275	0.755	-0.0002	Peppas
F5	0.885	0.062	0.835	-0.0002	0.924	0.135	0.992	0.168	0.217	0.537	-0.0001	Peppas
F6	0.732	0.084	0.611	-0.0006	0.951	0.147	0.989	0.207	0.194	0.621	-0.0002	Peppas
F7	0.716	0.049	0.425	-0.0002	0.949	0.1054	0.9591	0.152	0.372	0.825	-0.0000	Peppas
F8	0.833	0.142	0.875	-0.0015	0.963	0.1643	0.9997	0.196	0.291	0.757	-0.0005	Peppas
F9	0.841	0.092	0.735	-0.0007	0.937	0.1364	0.9979	0.132	0.109	0.533	-0.0003	Peppas

*R is drug release; k is rate constant for each model; n is diffusion coefficient; F: Formulation

Stability studies

Stability studies were conducted as per the ICH guidelines. The promising formulation F9 subjected to 40±2°C/75±5% RH for 1 mo

disclosed that there was no any significant changes in the colour, hardness, drug content uniformity, % CDR, and *in vitro* disintegration time. It specifies that prepared optimized formulation is stable [28]. The corresponding results are shown in the table 5.

Table 5: Stability studies of promising formulation F9

Time	Evaluation parameters					
	Colour	Hardness (kg/cm ²)	Drug content	Uniformity(mg)	<i>In vitro</i> disintegration time	% CDR
After 1 w	White	3.19±0.23	96.87±0.151		18.41±1.027	98.52
After 2 w	White	3.12±0.13	96.37±0.112		18.35±0.927	98.08
After 3 w	White	3.04±0.08	95.37±0.131		17.25±1.011	97.19
After 4 w	White	2.93±0.18	94.87±0.141		17.11±0.089	96.30

Data expressed in mean±SD, (n=3); CDR: Cumulative drug release

CONCLUSION

In the current efforts have been made to formulate and evaluate orodispersible tablets of propranolol hydrochloride using different super disintegrants by a direct compression method. The results disclosed that increased amount of various super disintegrants were associated with an increase in overall rate of cumulative drug release. Of all nine formulations, F9 formulation with 6 mg of crospovidone exhibited maximum cumulative drug release in 60 s. In addition, formulation F9 also showed short wetting time, good drug content, and fast disintegration and followed korsmeyer-peppas, as an ideal fitting model. Stability studies conducted also revealed no any significant changes in the colour, hardness, drug content uniformity, % CDR, and *in vitro* disintegration time. Henceforth, we concluded that formulated propranolol hydrochloride ODTs can be one of the better choices for the management of hypertension enhanced patient compliance and rapid onset of action.

ACKNOWLEDGEMENT

None

AUTHOR CONTRIBUTION

SPH designed the study and prepared the manuscript. CM developed and analysed the data and prepared the initial draft of the manuscript.

CONFLICT OF INTERESTS

The Author(s) declare(s) that they have no conflicts of interest to disclose

REFERENCES

1. Dey P, Maiti S. Orodispersible tablets: a new trend in drug delivery. *J Nat Sci Biol Med* 2010;1:2-5.
2. Nagar P, Singh K, Chauhan I, Verma M. Orally disintegrating tablets: formulation, preparation techniques and evaluation. *J Appl Pharm Sci* 2011;1:35-45.
3. Swamy N, Sachin, Abbas Z. Design and characterization of oral dispersible tablets of enalapril maleate using a co-processed excipient. *J Appl Pharm Sci* 2012;2:40-9.
4. Hirani JJ, Rathod DA, Vadalala KR. Orally disintegrating tablets: a review. *Trop J Pharm Res* 2009;8:161.
5. Abhay A, Swati A, Gayti A. Oral dispersible tablets: novel technology and development. *Int J Pharm Sci Rev Res* 2013;20:193-9.
6. Velmurugan S, Sundar V. Oral disintegrating tablets: an overview. *Int J Pharm Chem Sci* 2010;1:1-12.
7. Ibrahim HK, El-Setouhy DA. Valsartan orodispersible tablets: formulation, *in vitro/in vivo* characterization. *AAPS PharmSciTech* 2010;11:189-96.
8. Revathi S, Moulali SK, Dhanaraju MD. Formulation and evaluation of orodispersible valsartan tablets. *Pharm Lett* 2015;7:315-24.

9. Rewar S, Singh C, Bansal B, Pareek R, Sharma A. Oral dispersible tablets: An overview; development, technologies and evaluation. *Int J Res Dev Pharm Life Sci* 2014;3:1223-35.
10. Deshpande K, Ganesh N. Orodispersible tablets: an overview of formulation and technology. *Int J Pharma Biol Sci* 2011;2:726-34.
11. Sivaramaiah N, Alekhya M, Anusha M, Bhargav C, Harish G. Formulation and evaluation of oral dispersible tablets of propranolol hcl. *Am J Biol Pharm Res* 2014;1:160-9.
12. Mohsin A, Nimalakr NE, Sanaullah S, Aejaz A. Formulation and evaluation of mouth dissolving tablets of amitriptyline hydrochloride by direct compression technique. *Int J Pharm Pharm Sci* 2010;2:204-10.
13. Goyani SM, Shah P, Vyas B, Shah D. Formulation and evaluation of orally disintegrating tablets of meclizine hydrochloride. *Int Res J Pharm* 2012;3:196-9.
14. Leela MK, Ramana G, Diggpati R. Formulation and evaluation of oral disintegrated tablets of alfuzosin hydrochloride using super disintegrants. *J Appl Pharm Sci* 2011;1:161-5.
15. Vijaya K, Mishra D. Rapidly disintegrating oral tablets of meloxicam. *Indian Drugs* 2006;43:117 -21.
16. Hirave R, Kondawar M. Development and evaluation of herbal fast dissolving tablet of capparid divaricata lam. *Int J Adv Pharma* 2017;6:24-30.
17. Sai PB, Syamala S, Vinod kN, Voleti VK, Madhusudhan C. Formulation and evaluation of orodispersible tablets of clonazepam using natural super disintegrants. *IOSR-J Pharm Biol Sci* 2014;9:47-52.
18. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. *Acta Pol Pharm* 2010;67:217-23.
19. Gupta M, Vishal P. Formulation and evaluation oral dispersible tablets of cinnarizine. *J Drug Delivery Ther* 2013;3:12-7.
20. Karthik N, Vijaya KB, Sateesh KV. Different techniques to enhance the dissolution rate of lovastatin: formulation and evaluation. *Asian J Pharm Clin Res* 2013;6:56-60.
21. Reddy MNK, Hussain MA, Rao TR, Kishna TR, Pavan V. Formulation and evaluation of naproxen oral disintegrating tablets. *Int J Pharm Biol Sci* 2012;2:303-16.
22. Costa P, Sousa Lobo JM. Modeling and comparison of dissolution profiles. *Eur J Pharm Sci* 2001;13:123-33.
23. Sumit D, Sayantan M, Laxmi G. Preparation, characterization and evaluation of floating microparticles of ciprofloxacin. *Int J Appl Pharm* 2017;9:1-8.
24. Shashank C, Vipin KA, Anurag V, Navneet V, Sunil S. Comparative evaluation of natural and semisynthetic super disintegrants in the formulation of orodispersible tablets of norfloxacin. *Int J Pharm Pharma Sci* 2012;4:576-83.
25. Ananda K, Kiran KT, Gyana JR. Development, formulation and evaluation of solifenacin succinate immediate release oral tablets by using starch and hpmc. *Int J Res Pharm Nano Sci* 2013;2:91-100.
26. Mangesh MS, Nagesh ST. Formulation and *in vitro* evaluation of fast dissolving tablets of metoprolol tartrate. *Braz J Pharm Sci* 2013;49:784-92.
27. Chandrasekhar P, Shahid MS, Niranjan BM. Formulation and evaluation of oral dispersible tablets of antihypertensive drug atenolol. *Int J Pharm* 2013;3:79-84.
28. Parag P, Tejal P, Rajesh P. Formulation and evaluation of mouth dissolving tablet for the antihypertensive drug. *Pharmagene* 2013;1:10-20.