Available online on 15.01.2020 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Formulation and evaluation of chewable tablets of Desloratadine prepared by aqueous and non-aqueous techniques

Abbas Muhammad [1*], Abbas Musharraf [2], Tariq Fatima [3], Yasin Rabiya [4], Nabeel Muhammad [5]

[1*] Assistant Professor, Islam College of Pharmacy, Sialkot, Pakistan

[2] Lecturer, Lahore Pharmacy College, Lahore, Pakistan

[3] Student, College of Pharmacy, University of Sargodha, Sargodha, Pakistan

[4] Student, Lahore Pharmacy College, Lahore Pakistan

ABSTRACT

In the modern era, chewable tablets are preferred over conventional dosage forms by pediatric, geriatric and bedridden patients due to difficulty in swallowing, lesser amount of water for swallowing medications as well as unable to tolerate the bitter taste of certain drugs. Chewable tablets of Desloratadine (DS) were formulated by aqueous and non-aqueous granulation method using water paste and Isopropyl alcohol (IPA) as a wetting agents respectively. Desloratadine is used to treat the symptoms of allergy such as sneezing, watery eyes. In the recent research, we have formulated eight trials by various concentrations of excipients. For instance; lactose, talcum, magnesium stearate, blue color, flavor, aspartame, mannitol, avicel 101 and polyvenylpyrollidine (PVP). Pre-compression and post compression parameters (thickness, hardness, friability weight variation and drug content) of the formulations were evaluated. B_3 was our optimum dosage form because its Hausner's ratio, compressibility index, bulk density, tap density, angle of repose have optimum values i.e. 1.01, 5.1%, 0.66(g/cc), 0.69(g/cc), 26.1º respectively and post-compression i.e. thickness, hardness, friability weight variation and drug content have values, 2.9mm, 3.9(kg/cm^2), 0.6%, 99.5% respectively. Tablets prepared by wet granulation technique showed reasonable release profile i.e. 100% within the required time i.e. 2 hours. Moreover, organoleptic evaluation of all formulations were performed.

Keywords: Desloratadine, chewable, magnesium stearate, aspartame, compressibility, granulation.

Article Info: Received 09 Nov 2019; Review Completed 11 Dec 2019; Accepted 14 Dec 2019; Available online 15 Jan 2020

Cite this article as:

Abbas M, Abbas M, Tariq F, Yasin R, Nabeel M, Formulation and evaluation of chewable tablets of Desloratadine prepared by aqueous and non-aqueous techniques, Journal of Drug Delivery and Therapeutics. 2020; 10(1):5-10
http://dx.doi.org/10.22270/jddt.v10i1.3796

***Address for Correspondence:**

Muhammad Abbas, Islam College of Pharmacy, Pasrur Road, Sialkot-51040, Pakistan

INTRODUCTION

Chewable tablets are the tablets which are required to be broken and chewed in between the teeth before ingestion. Some children have difficulty in swallowing especially pediatric, geriatric and bedridden patients.Selection of suitable ingredients during manufacturing a robust solid dosage form is required during development of formulations. The critical step is the selection of appropriate excipients with minimum disintegration time and maximum bioavailability during design of solid dosage form. Chewable tablets are intended to disintegrate smoothly in mouth at a moderate rate either with or without actual chewing. Characteristically chewable tablets have a smooth texture and pleasant taste upon disintegration[1]. Antihistamines are used as first-line therapy for the treatment of allergic rhinitis[2]. At present, most of signs and symptoms of allergic rhinitis are treated by available antihistamines, but they are not measured to be very effective for the management of congestion[3]. Therefore, antihistamines are frequently administered along with decongestant to reduce nasal obstruction. Consumption of antihistamines is minimized due to their adverse effects. For instance, use of diphenhydramine and chlorpheniramine is condensed as compared to new agents i.e. cetirizine and azelastine, however, it may causes sedation and psychomotor impairment[4]. Another newer agents i.e. terfenadine and astemizole have severe adverse effects e.g. persistence of the QTC interval and cardiac arrhythmias[5]. Uses of several antihistamines have also been decreased due to drug and food interactions. For example, plasma concentrations of terfenadine and astemizole may be increased, when these agents are administered concomitantly with cytochrome P450 inhibitors such as; erythromycin and ketoconazole[5]. It has been suggested that plasma levels of fexofenadine may

be changed due to simultaneous administration of erythromycin and ketoconazole, which are drug transporters inhibitors or inducer, such as the organic anion transport polypeptide (OATP) or P-glycoprotein (P-gp)[6]. On the other side, serum concentration of cetirizine is decreased when the product is administered with food[5]. Desloratadine is a new antihistaminic compound, which is active metabolite of loratadine. It is approximately 10 to 20 times more potent at H_1-receptor binding than loratadine *in-vitro* and 2.5 to 4 times more antihistaminic potency in animals[7]. Desloratadine was also shown to have a significantly longer elimination half-life than loratadine[8].

MATERIALS AND METHODS

Materials

Desloratadine (raw material) was gifted by Wimits Pharmaceuticals Pvt Ltd. Lactose, talc, magnesium stearate, mannitol were purchased from Sigma-Aldrich (Germany). Aspartame, PVP, IPA, Avicel 101 were purchased from Midland Scientific Inc.

Methods

Characterization of drug-superdisintegrants

Fourier transform infrared spectroscopy was used to find the physicochemical compatibility between the active pharmaceutical ingredient with excepients used in chewable tablets[9]. In this method, spectra of pure drug (Desloratadine) and excipients in combination were taken. KBr press (1mg of sample in 300mg KBr) was used to prepare transparent pallets by applying hydraulic pressure of 8000-20000 psi on a pulverized mixture of sample with KBr. Scanning range of infrared is 4000-400 cm^{-1} and the resolution was $2cm^{-1}$. Compatibility between drug and excipients were evaluated by comparing their FTIR spectra with reference spectra of pure drug[11].

Micromeritic properties of formulation powder blends

Powder blends were prepared according to the quantity mentioned in **Table 1** to analyze the flowability and compressibility of desired formulations. Angle of repose, bulk density, tapped density, hausner's ratio, and carr's index was calculated to understand the micromeritic properties of powder blends. Angle of repose demonstrates the flow properties of the powder blend and was determined by funnel method. In this method, Powder blend was filled in the funnel and placed 2cm above the smooth surface. Accurately weighed powder blend was poured from a funnel in such a way that maximum cone height (h) obtained and funnel should not exceed more than 1cm above the cone height (h)[10]. Angle of repose was calculated by using the following formula.

$$\theta = \tan^{-1} (h / r) \ldots\ldots \text{(Eq1)}$$

Where "**h**" is the height and "r" radius of the powder cone.

Apparent bulk density, tapped density was measured by the graduated cylinder method and in g/mL and hausner ratio was calculated by using following formula.

$$\text{Hausner ratio} = \text{Tapped density} / \text{Bulk density} \ldots\ldots \text{(Eq2)}$$

The extent of compressibility of powder blends was determined by measuring apparent bulk density and tapped density and Carr's index was calculated by following formula.

$$C = \text{Tapped density} - \text{Bulk density} / \text{Tapped density} \times 100$$

Preparation of chewable tablets

Chewable tablets of desloratadine were prepared by using aqueous granulation and non-aqueous granulation method.

Aqueous Method:

In this method, active ingredient i.e. desloradine was mixed with lactose, avicel 101 and mannitol. Add 10ml of 10% PVP and mix, until wet damp mass was formed. Then passed damp mass from sieve no.12 and granules were formed. Dry these granules in oven at 50˚C for 30 minutes. Then mix it with sweetening agent (Mannitol or Aspartame), flavoring agent, coloring agent, magnesium stearate and talc. Tablets were formed by using single punch machine equipped with 15mm punch and die[11].

Non-Aqueous Method:

In this method, active ingredient i.e. desloradine was mixed with lactose, avicel 101 and mannitol. Add 10%PVP in isopropyl alcohol solution and formed granules. Dried these granules in hot air oven at 40-50˚C. Then again pass these granules from sieve No. 22. After this, mix it with sweetening agent (Mannitol or Aspartame), flavoring agent, coloring agent, magnesium stearate and talc. Then this mixture was tested for evaluation of the flow properties and made tablets by using single punch machine[11].

Composition of formulations is shown in the **Table 1.**

Table 1: Composition of one tablet of different batches

Batches Numbers		T1	T2	T3	T4	T5	T6	T7	T8
Chemical Name		(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)
1	Desloratadine	5	5	5	5	5	5	5	5
2	Lactose	164.03	164.03	164.03	164.03	152.03	152.03	152.03	152.03
3	Aspartame	12	12	_	_	24	24	_	_
4	Mannitol	_	_	12	12	_	_	24	24
5	Avicel 101	2	2	2	2	S2	2	2	2
6	PVP	5.3	5.3	5.3	5.3	5.3	5.3	5.3	5.3
7	Talc	3.73	3.73	3.73	3.73	3.73	3.73	3.73	3.73
8	Magnesium Stearate	3.07	3.07	3.07	3.07	3.07	3.07	3.07	3.07
9	Blue Color	0.23	0.23	0.23	0.23	0.23	0.23	0.23	0.23
10	Flavor	4.61	4.61	4.61	4.61	4.61	4.61	4.61	4.61
11	IPA	_	0.12ml	_	0.12ml	_	0.12ml	_	0.12ml
12	Distilled Water	q.s	_	q.s	_	q.s	_	q.s	_

Each Tablet contains: Desloratadine USP …….. 5mg **Batch Size:** 200 Tablets

Characterization of prepared tablets

Tablet Hardness

It is used to determine hardness of the tablets. It is measured by selection of randomly three tablets from each formulation T1-T8 and placed them horizontally between two arms of digital hardness tester (MH-L Galvano Scientific). Breaking force is applied until the tablet is broken down. Note the value of hardness in kg/cm^2.

Tablet Thickness and Diameter

It is used to verify thickness and diameter of tablets, place the tablet vertically between two arms of the digital apparatus (Pharma Test Germany) and note the values that appear on the screen of instrument.

Weight variation

This test is used to determine individual weight variation of tablets from an average weight in order to determine the consistency in uniformity of the batch. From each formulation 20 tablets were selected randomly and weighed on an analytical balance (Shimadzu, Japan). Weight variation was calculated according to British Pharmacopeia specifications.

Friability

Friability of tablets were analyzed by randomly selecting 10 tablets and placed them in a plastic chamber of Rosch Friabilator. The friabilator drum was rotated at 25 rpm for 4 minutes. The percentage loss in the weight of tablets was calculated by the following formula.

%age Friability = Initial weight – Final weight / initial weight* x *100

Drug content determination

The assay of randomly selected 10 tablets from each batch was conducted to determine the content of Desloratadine. For this purpose, standard stock solution of pure of desloratadine was prepared and then further serial dilutions (0.01mg/ml – 0.05mg/ml) were prepared from it. Measure the absorbance of the solution at 248nm on UV-visible spectrophotometer (PG instruments Ltd) and distilled water using as blank. Determine drug content by using given equation[12].

% age content = absorbance of sample/absorbance of standard x 100

Percentage drug release

The dissolution test is used to evaluate the release of a drug from its formulation in a desired manner. To perform dissolution test we used Paddle Apparatus. Filled each 900ml volume with dissolution medium (0.1N HCL) and set the temperature 37ºC. Then placed 1 tablet in each beaker and took sample after different time intervals (30, 60, 90 and 120 minutes) and tested under UV spectrophotometer to find out the percentage of drug dissolved in medium with respect to reference solution i.e. Desloratadine solution[13].

Organoleptic evaluation:

It is used to determine the taste of the dosage forms by means of our senses. It includes the macroscopic appearance of the drug, its odor and taste, rarely the sound of its fracture and the appearance of the drug to touch. Took 20 healthy volunteers, having appropriate sense of taste and ask them to chew the tablets and evaluate on the basis of following table[14].

Specifications of Organoleptic evaluation are shown in the **Table 2:**

Table 2: Organoleptic evaluation scale

Category	Scale
Very Sweet	5
Sweet	4
Neutral	3
Bitter	2
Very Bitter	1

RESULTS

Characterization of drug-superdisintegrants

FTIR results of pure drug i.e. Desloratadine and optimum dosage form (B3) had shown that all characteristics peaks of Desloratadine were appeared in B3. It shows that there were no interactions between excipients and desloratadine. Their FTIR spectra as shown in **Figure 1.**

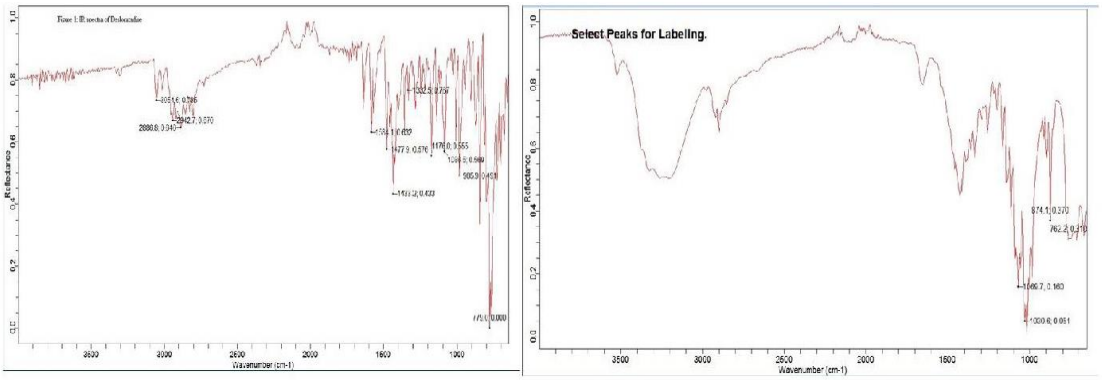

Fig 1: FTIR Spectra

Micromeritic properties of formulation powder blends

The bulk and tapped density, compressibility index and Hausner's ratio of all batches were within the range (less than 1%) as shown in the **Table 3.**

Table 3: Micromeritics evaluation of powder blend*

Code	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio	Angle Of Repose (Θ)	Flowability
T1	0.76 ± 0.010	0.8 ± 0.013	5 ± 0.894	1.05 ± 0.028	28.5 ± 1.022	Excellent
T2	0.71 ± 0.012	0.73 ± 0.024	2.7 ± 0.828	1.02 ± 0.016	27.3 ± 0.372	Excellent
T3	0.66 ± 0.021	0.69 ± 0.058	4.3 ± 0.161	1.04 ± 0.013	26.1 ± 0.920	Excellent
T4	0.72 ± 0.0360	0.77 ± 0.014	4.2 ± 0.974	1.07 ± 0.097	29 ± 0.635	Excellent
T5	0.68 ± 0.012	0.79 ± 0.007	4.9 ± 0.501	1.06 ± 0.094	28.9 ± 0.375	Excellent
T6	0.73 ± 0.047	0.73 ± 0.060	4.8 ± 0.859	1.05 ± 0.011	27.6 ± 0.534	Excellent
T7	0.74 ± 0.114	0.78 ± 0.152	4.6 ± 0.661	1.03 ± 0.063	28.2 ± 1.045	Excellent
T8	0.7 ± 0.013	0.75 ± 0.033	4.5 ± 0.706	1.04 ± 0.013	28.1 ± 0.870	Excellent

Characterization of prepared tablets

All the formulations showed similar thickness. Moreover, friability, hardness, weight variation of all the trials were found to be within the official limits as shown in the **Table 4.**

Table 4: Characterization of tablets of all formulations

Sr#	Batch No	Hardness (kg/cm^2)	Friability (%)	Weight Variation (%)	Thickness (mm)
1	T1	3.23	0.9	99.6±0.32	2.9±0.2
2	T2	3.01	0.7	99.8±0.99	2.8±0.2
3	T3	2.98	0.8	99.7±0.01	2.9±0.2
4	T4	4.5	0.9	98.9±0.14	2.8±0.2
5	T5	4.3	0.8	100.2±0.65	2.8±0.2
6	T6	3.2	0.9	99.6±0.74	2.9±0.2
7	T7	4.1	0.8	99.8±0.41	2.9±0.2
8	T8	3.9	0.7	99.9±0.11	2.9±0.2

Percentage content of prepared tablets

The assay of drug was performed using UV-Spectrophotometer at wavelength 280nm, using 0.1N HCl as blank solution. All the formulations were within the specification (95-105%) as per USP. The B3 is considered as more optimized formulation as shown in the **Table 5.**

Table 5: Percentage content

Sr#	Batch No	Percentage purity (%)
1	T1	97.45
2	T2	96.1
3	T3	99.2
4	T4	95.2
5	T5	96.3
6	T6	97.08
7	T7	97.09
8	T8	95

Percentage drug release

Percentage cumulative drug release of all 8 formulations of Desloratadine chewable tablets were under the specification as shown in the **Table 6** and **Figure 2**.

Table 6: Release Profile all formulations (%)

Sr#	Batch No	Time(30mins) %drug	Time(60mins) % drug	Time(90mins) % drug	Time(120) % drug
1	T1	75	85	90	94
2	T2	78	81	89	95
3	T3	84	89	91	101
4	T4	72	79	88	96
5	T5	80	85	91	93
6	T6	79	83	91	92
7	T7	82	88	95	92
8	T8	81	89	94	90

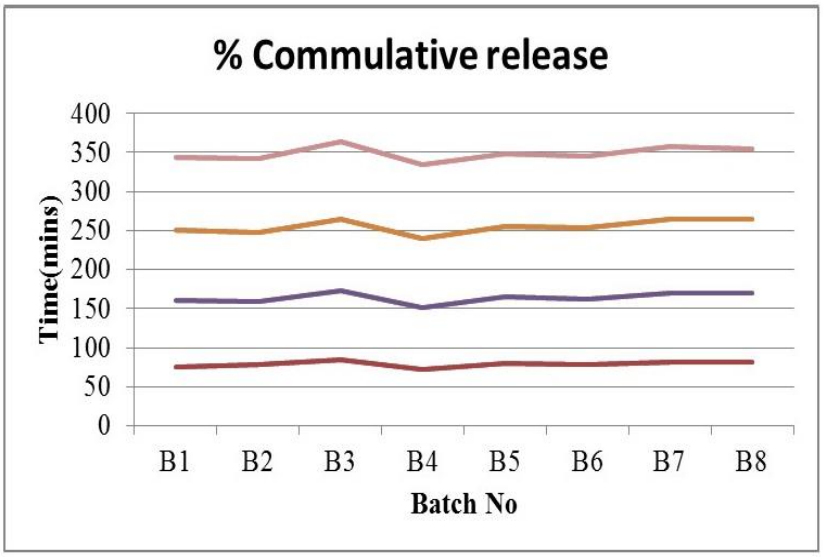

Fig 2: Percentage cumulative drug release of 8 formulations of Desloratadine chewable tablets

DISCUSSION

Characterization of drug-superdisintegrants

FTIR spectra of active pharmaceutical ingredient showed the main characteristic peaks between 500-1700 cm^{-1}. The figure shows also alkene (C=C stretch (conjugated)) at 1610-1640 cm^{-1}, imines (R2C=N-R stretch) at 1640-1690 cm-1, aromatic (C=C stretch) at 1475 cm^{-1} and 1600 cm^{-1}, (C-H stretch) at 3000-3020 cm^{-1}, alkanes (C-H stretch) at 2800-2950 cm^{-1} , and amines (N-H bend) 3300-3500 cm^{-1}. Characteristic peaks of pure drug appeared in all formulations indicates the absence of any interaction with the excipients material. Since there was no disappearance or change in position of the absorption bands characteristic for the drug, which demonstrates the compatibility between active ingredient and excepients used during formulation of chewable tablets with aqueous and non- aqueous techniques.

Micromeritic properties of formulation powder blends

The compressibility index for all the formulations was found to be within the range 2-5, which indicates the excellent properties, the flow properties were further analyzed by determining the angle of repose, which were within the range of 28 to 30°. The Hausner's ratio for all the granules formulated are less than 2%, indicating free flow property. B3 was our optimum dosage form on the basis of bulk density, tapped i.e. 0.71, 0.81 respectively as shown in the **Table 3**.

Characterization of prepared tablets

Tablets from different formulations showed hardness in the range of 2.98-3.9 Kg/cm2.The friability value is less than 1% all formulations were well within the range.

All batches passed the USP requirement in terms of weight variation and drug uniformity as shown in the **Table 4**.

Organoleptic evaluation of tablets

The Studies have shown that taste of formulations have been efficiently masked especially the tablets prepared by aqueous granulation method as shown in the **Figure 3.**

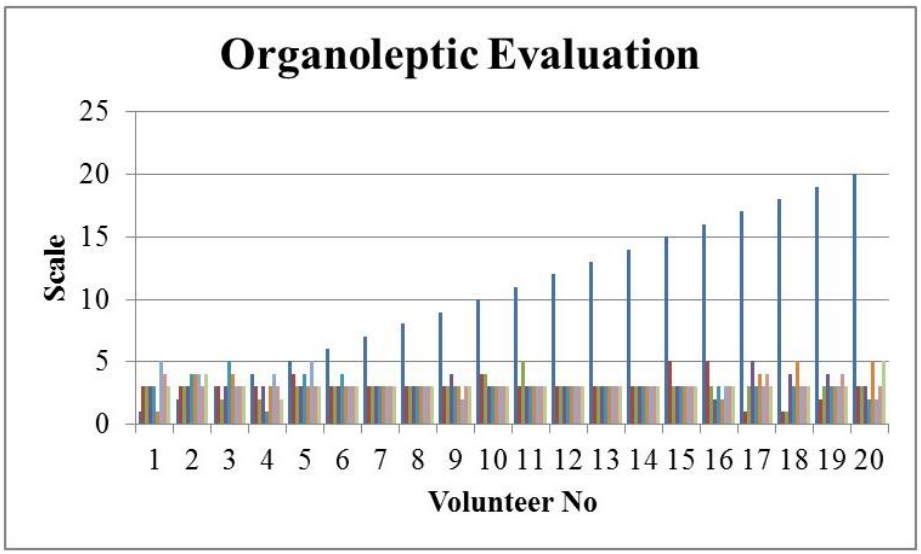

Fig 3: Taste of tablets efficiently masked

CONCLUSION

From the recent research, it is concluded through FTIR studies that there was no interaction between active pharmaceutical ingredient and excipients, so the drug is compatible with other excipients. Granules showed excellent flow properties and micromeritics parameters of granules were found within official limits. The compressibility index for all formulations was found to be within the range 2-5. The formulated dosage form did not exhibit any sticking, capping, edging, lamination and other defects. Post compression parameters such as hardness, thickness, friability and dissolution time were according to specifications. Dissolution rates of chewable tablets prepared by aqueous granulation technique were better than tablets prepared by non-aqueous techniques.

CONFLICT OF INTEREST

Authors have no conflict of interest to report.

ACKNOWLEDGEMENT

Authors like to acknowledge Lahore Pharmacy College for providing their research facilities to conduct this project.

REFERENCES

1. Udaykumar M et al: Fast Dissolving Tablets: New Fangled Drug Delivery System, A Comprehensive Review. International Journal of Research in Drug Delivery, 2012; 2(3):15-18.
2. Dykewicz MS et al:Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. Annals of Allergy, Asthma & Immunology, 1998; 81(5):478-518.
3. Van CP et al: Consensus statement on the treatment of allergic rhinitis. Allergy, 2000; 55(2):116-134.
4. Gonzalez M and Estes K. Pharmacokinetic overview of oral second-generation H1 antihistamines. International journal of clinical pharmacology and therapeutics, 1998; 36(5):292-300.
5. Geha RS and MeltzerEO. Desloratadine: a new, nonsedating, oral antihistamine. Journal of Allergy and Clinical Immunology, 2001; 107(4):751-762.
6. Cvetkovic M et al: OATP and P-glycoprotein transporters mediate the cellular uptake and excretion of fexofenadine. Drug metabolism and disposition, 1999; 27(8):866-871.
7. Kreutner W et al: Preclinical Pharmacology of Desloratadine, a Selective and Nonsedating Histamine H1 Receptor Antagonist2nd Communication: Lack of central nervous system and cardiovascular effects. Arzneimittelforschung, 2000; 50(05):441-448.
8. Affrime M et al: A pharmacokinetic profile of desloratadine in healthy adults, including elderly. Clinical pharmacokinetics, 2002; 41(1):13-19.
9. Lakshmanan S and PandeyM. Analysis of startup oscillations in natural circulation boiling systems. Nuclear Engineering and Design, 2009; 239(11):2391-2398.
10. Nazir T. Extended Release Orally Disintegrating Dosage Forms are Potential Techniques to Deliver and Maintain the Therapeutic Ranges of Plasma Drug Concentrations. J App Pharm, 2015; 7:001.
11. Kandi M et al: Formulation and Evaluation of Chewable Tablet of Metformin HCl Using Stevia by Different Techniques. International Journal of PharmTech Research, 2013; 5(3):1364-1372.
12. Radke R, JadhavJ and ChajeedM. Formulation and evaluation of orodispersible tablets of baclofen. Int J Chem Tech Res, 2009; 1(3):517-21.
13. Chandrasekaran A et al: Post market in vitro equivalency evaluation of paracetamol tablets in kedah, Malaysia. Int J Pharm Sci Nanotech, 2011; 4(2):1403-1407.
14. Etman MA et al: Formulation of Desloratadine Oral Disintegrating Tablets. Journal of Applied Pharmaceutical Science, 2014; 4(11):054-061.