Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 4, 2013

Research Article

FORMULATION AND EVALUATION OF LEVO CITERIZINE DIHYDRO CHLORIDE FAST DISSOLVING TABLETS USING SUPERDISINTEGRANTS

VIJAYA KUMAR VOLETI*, V.GUNASEKHARAN, SAI PADMINI BOLLA, JUNJU MOHAN KUMAR, MOUNICA RAYAPROLU

Department of pharmaceutics, Rao's College of Pharmacy, Nellore, A. P, India. Email: vijay66vvk@gmail.com

Received: 15 July 2013, Revised and Accepted: 23 Aug 2013

ABSTRACT

Objective: The low oral bioavailability of levocetirizine dihydrochloride due to its high first pass metabolism, led to the formulation development of fast dissolving tablets that disintegrate with-in seconds in oral cavity.

Methods: Levocetirizine dihydrochloride (5mg) fast dissolving tablets were prepared by direct compression technique using three synthetic superdisintegrants in different proportions. Development of the formulation in the present study was mainly based on the type and concentration of polymers and the properties of the drug.

Results: FTIR studies showed that the polymers are compatible. The evaluation tests like thickness, weight variation, hardness, friability, In vitro dispersion Time, Wetting time & Water absorption ratio, Drug content determination, In vitro drug release were studied. The *in vitro* release of optimized formulation PF-9 was found to be 99.81% within 10 min. and the *in vitro* dispersion time being 1sec.

Conclusion: The formulation containing 2.5% cros carmallose sodium (PF-9) was identified as ideal and better formulation among all formulations developed for Levocetirizine dihydrochloride tablets.

Keywords: Levocetirizine dihydrochloride, Fast dissolving tablets, dire@ct compression, Synthetic super disintegrants.

INTRODUCTION

Oral administration owns the advantages like ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates) and most importantly, patient compliance. Also, solid oral delivery systems do not require sterile conditions and therefore, less expensive to manufacture. Several novel technologies for oral delivery have recently become available to address the physicochemical and pharmacokinetic characteristics of drugs, while improving patient compliance**[1]**. The basic disadvantage of conventional tablets is the high first pass metabolism which can be overcome by designing fast dissolving tablets (FDT). The FDT's also known as oro-dispersible tablets does'nt require water to swallow**[2,3]**, disintegrate in the mouth, has the ease of administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric and psychiatric patients, allows the manufacture of tablet using conventional processing and packaging equipment at low cost**[4]**.

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution by swelling, wicking and effervescent actions. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

Direct compression is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

Levocetirizine dihydrochloride, have low oral bioavailability due to high first pass metabolism. To minimize such problems levocetirizine dihydrochloride is formulated in the form of fast dissolving tablets where the drug is rapidly disintegrated in mouth within fraction of seconds and improves the oral drug bioavailability.

Hence, in the present study an attempt has been made to formulate and evaluate fast dissolving tablets of Levocetirizine dihydrochloride by direct compression method using three super disintegrants.

MATERIALS

Levocetirizine dihydrochloride from Aurabindo Labs, Sodium starch glycolate Crosscarmellose sodium, Crospovidone from Shreeji chemicals, Mumbai, Microcrystalline cellulose, Mannitol, Magnesium sterarte, Potassium dihydrogen orthophosphate, and Sodium hydroxide and Raspberry flavor are of analytical grade.

Preparation of Levocetirizine dihydrochloride fast dissolving Tablets:

Levocetirizine dihydrochloride fast dissolving tablets were formulated by using the ingredients SSG, CP and CCS. All the ingredients with drug except Magnesium stearate were taken in the mortar. The powder blend was mixed well by using mortar and pestle for 15 to 30 minutes, and then mixture was passed through # 80 sieve. Finally Magnesium stearate was added as lubricant and mixed thoroughly. The powder blend was compressed using 16 stations tablet compression machine (Cadmach JMD-4-8, Ahemdabad, India) to produce tablets of Levocetirizine dihydrochloride weighing 120mg having diameter of 8 mm. . The formulations PF1-PF4 were formulated with the help of sodium starch glycolate in concentration 2.5, 5, 7.5, 10% respectively . The formulations PF5-PF8 were formulated with the help of crospovidone in concentration 2.5, 5, 7.5, 10 respectively and the formulations PF9-PF12 were formulated with the help of croscarmallose sodium in concentrations 2.5, 5, 7.5, 10% respectively.

EVALUATION

Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.[5]The results were tabulatedin table no.2

Hardness Test

A significant strength of ODT is difficult to achieve due to the specialized processes and ingredients used in the manufacturing. The limit of hardness for the ODT is usually kept in a lower range to facilitate early disintegration in the mouth. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester. **[6]**

Friability Test

It is not an official method but required for the shipment of the product. It is carried out by using Friabilator. The 10 or 20 tablets were weighed initially and transferred into a Friabilator and allowed to rotate 100 rotations. After the completion tablets were weighed. The % friability was calculated using the equation,

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

Uniformity of weight

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity**[7,8]** .

In-vitro dispersion time

In-vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of sorenson's buffer pH 6.8. Three tablets from each formulation was randomly selected and in-vitro dispersion time was performed **[9,10]**.

Wetting time [11]and water absorption ratio

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet as put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to equation:

R = 100 (Wa - Wb)/Wb

Where Wb and Wa are the weights of tablet before and after water absorption, respectively

Drug content determination

Procedure of determining drug content

Three uncoated tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately weighed amount of tablet powder was taken from the crushed blend. Then the samples were transferred to three 100 ml volumetric flasks and were diluted up to the mark with phosphate buffer (pH 6.8) solution. The contents were shaken periodically and kept for 24 hours for solvation of drug completely. The mixtures were filtered, appropriately diluted, and absorbences were measured at λmax 229.50 nm against blank reference. The drug content in each tablet was calculated using the standard calibration curve of Levocetirizine dihydrochloride in phosphate buffer pH 6.8 solution.

In vitro drug release

In vitro drug release of the samples was carried out using USP – type II dissolution apparatus (paddle type). The dissolution medium, 900 ml of phosphate buffer (pH 6.8) solution, was placed into the dissolution flask maintaining the temperature of 37±0.5ºC and rpm of 50. One tablet was placed in each flask of dissolution apparatus. The apparatus was allowed to run for 10 min. Samples measuring 5 ml were withdrawn after every 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 min. Samples were filtered through 10 µm filter. The fresh dissolution medium was replaced every time to maintain sink condition. The collected samples were analyzed at 229.50 nm using dissolution medium as blank. The cumulative percentage drug release was calculated.

Table 1: Formulation design of Levocetirizine dihydrochloride fast dissolving tablets

S. No.	Ingredients	F1 mg	F2 mg	F3 mg	F4 mg	F5 mg	F6 mg	F7 mg	F8 mg	F9 mg	F10 mg	F11 mg	F12 mg
1	Levocetirizine dihydrochloride	5	5	5	5	5	5	5	5	5	5	5	5
2	Sodium Starch Glycollate	3	6	9	12	-	-	-	-	-	-	-	-
3	Crospovidone.	-	-	-	-	3	6	9	12	-	-	-	-
4	Cross caramellose Sodium	-	-	-	-	-	-	-	-	3	6	9	12
5	Mannitol	20	20	20	20	20	20	20	20	20	20	20	20
6	Aerosil	2	2	2	2	2	2	2	2	2	2	2	2
7	Magnesiumstearate	1	1	1	1	1	1	1	1	1	1	1	1
8	Aspartame	10	10	10	10	10	10	10	10	10	10	10	10
9	Flavour(orange)	4	4	4	4	4	4	4	4	4	4	4	4
10	Microcrystalline cellulose	75	72	69	66	75	72	69	66	75	72	69	66
11	Total weight	120	120	120	120	120	120	120	120	120	120	120	120

Table 2: Postcompression parameters of Levocetirizine dil. HCl tablets

Formula Code	*In vitro dispersionTime (sec)	*Wetting time (sec)	*Water Absorption Ratio	*Thickness (mm)	*Hardness (kg/cm²)	Friability (%)	Weight Variation
PF1	19±1.527	22±1.52	109.06±0.60	2.49±0.02	3.14±0.25	0.234±0.07	120.0±0.20
PF2	22±1.527	24±1.73	100.60±0.91	2.48±0.02	3.69±0.25	0.296±0.07	119.8±0.33
PF3	24±1.527	28±1.00	96.38±0.49	2.48±0.01	3.12±0.27	0.348±0.04	119.4±0.21
PF4	34±1.341	36±1.00	87.44±0.91	2.47±0.01	3.20±0.25	0.376±0.04	120.33±0.76
PF5	26±1.000	30±1.52	97.20±0.03	2.44±0.01	3.47±0.27	0.336±0.13	119.6±0.34
PF6	32±1.527	38±1.72	92.10±0.26	2.43±0.01	3.51±0.25	0.376±0.04	120.0±0.12
PF7	36±1.527	44±1.52	91.07±0.86	2.43±0.01	3.12±0.27	0.336±0.14	118.96±0.28
PF8	50±1.527	61±1.52	85.63±0.13	2.45±0.01	3.20±0.25	0.227±0.03	118.3±0.71
PF9	12±1.154	14±1.52	119.53±0.31	2.45±0.01	3.50±0.27	0.309±0.05	120.1±1.27
PF10	13±1.527	21±1.52	115.00±0.23	2.44±0.01	3.34±0.25	0.339±0.07	120.65±0.20
PF11	21±1.527	25±1.52	107.00±0.54	2.45±0.01	3.66±0.25	0.321±0.01	118.96±0.48
PF12	28±1.527	34±1.52	99.26±0.03	2.46±0.01	3.20±0.25	0.310±0.07	119.32±1.26

Table 3: In vitro drug release profile of Levocetirizine diHCl tablets

Time (mins)	0	2	4	6	8	10
PF1	0	48.23 ±0.65	65.45 ± 1.12	76.32 ±1.23	87.42 ±0.76	98.02 ±0.41
PF2	0	38.87 ±0.22	56.87 ±1.12	68.40 ±1.23	76.65 ±0.76	88.51 ±0.33
PF3	0	41.67 ±0.96	61.12 ±0.54	70.54 ±0.43	80.78 ±0.54	91.75 ±0.33
PF4	0	37.28 ±0.87	49.32 ±1.15	60.22 ±0.37	71.73 ±0.62	80.27 ±0.21
PF5	0	48.86 ±0.45	64.45 ±1.12	74.32 ±1.23	86.42 ±0.76	98.62 ±0.21
PF6	0	42.67 ±0.96	62.12 ±0.54	71.54 ±0.43	81.78 ±0.54	92.15 ±0.44
PF7	0	39.17 ±0.22	56.87 ±1.12	68.40 ±1.23	76.65 ±0.76	89.51 ±0.33
PF8	0	38.28 ±0.87	47.22 ±0.37	60.22 ±0.37	73.73 ±0.62	83.30 ±0.42
PF9	0	48.861 ±.0.0	63.120 ±.62	80.43 ±0.91	89.90 ±0.47	99.81 ±0.01
PF10	0	44.76 ±0.12	55.87 ±0.18	72.50 ±1.32	84.92 ±1.12	94.00 ±0.38
PF11	0	46.72 ±0.12	59.98 ±0.54	75.65 ±0.32	89.64 ±0.65	94.00 ±0.38
PF12	0	37.16 ±0.87	49.32 ±1.15	62.22 ±0.37	75.73 ±0.62	86.75 ±0.42

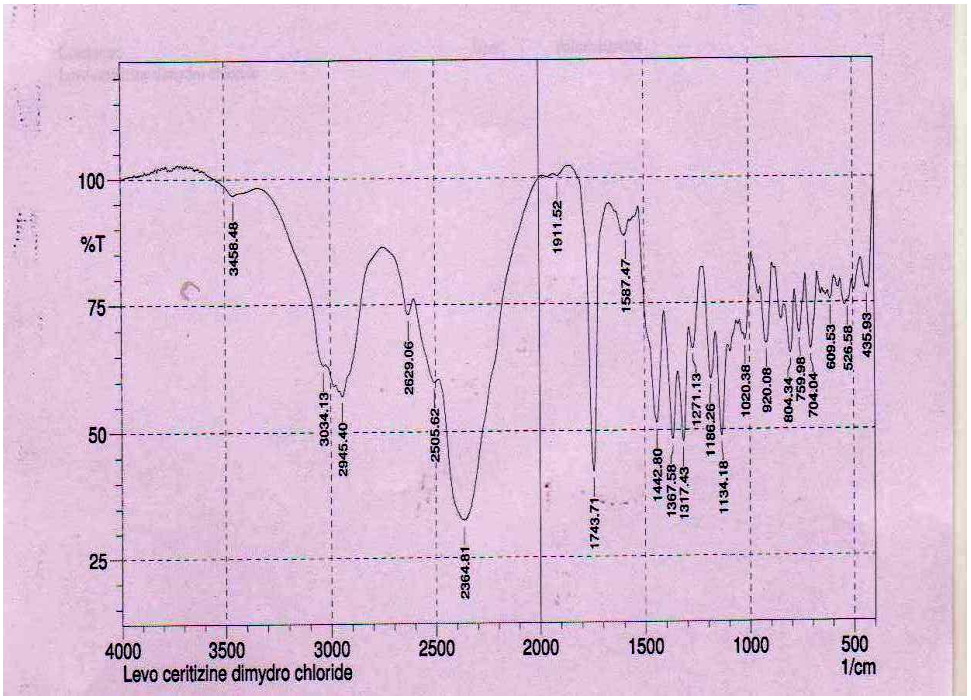

Fig. 1: IR spectra of Levocetirizine diHCl

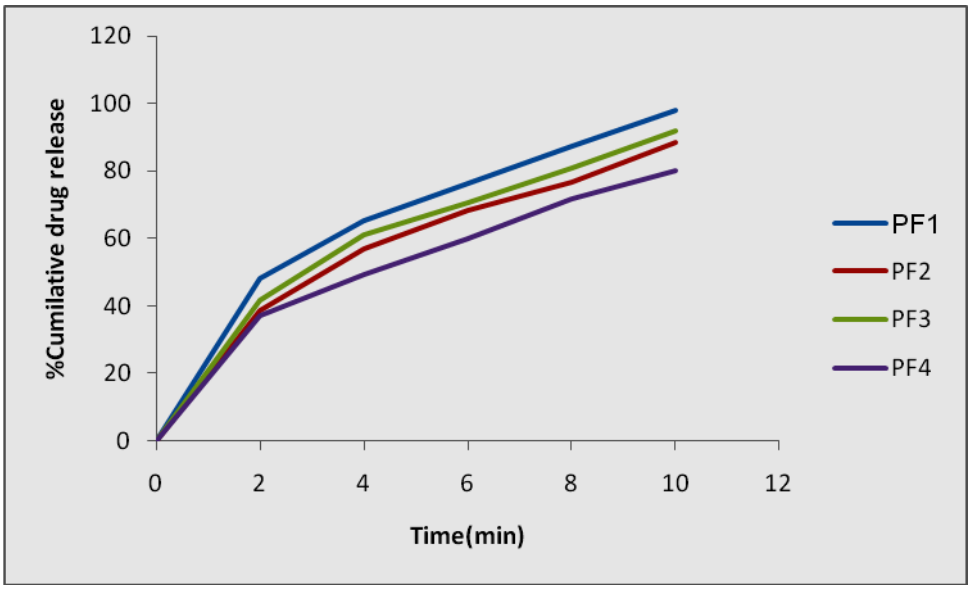

Fig. 2: In vitro drug release profile of Levocetirizine di HCl tablets containing SSG and CP(PF1-PF4)

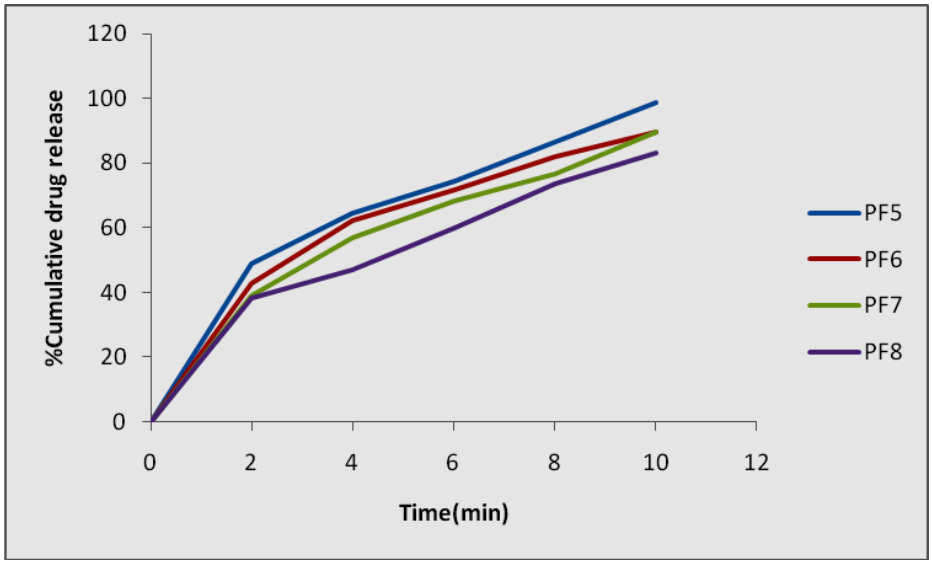

Fig. 3: In vitro drug release profile of Levocetirizine di HCl tablets containing SSG and CCS(PF5-PF8)

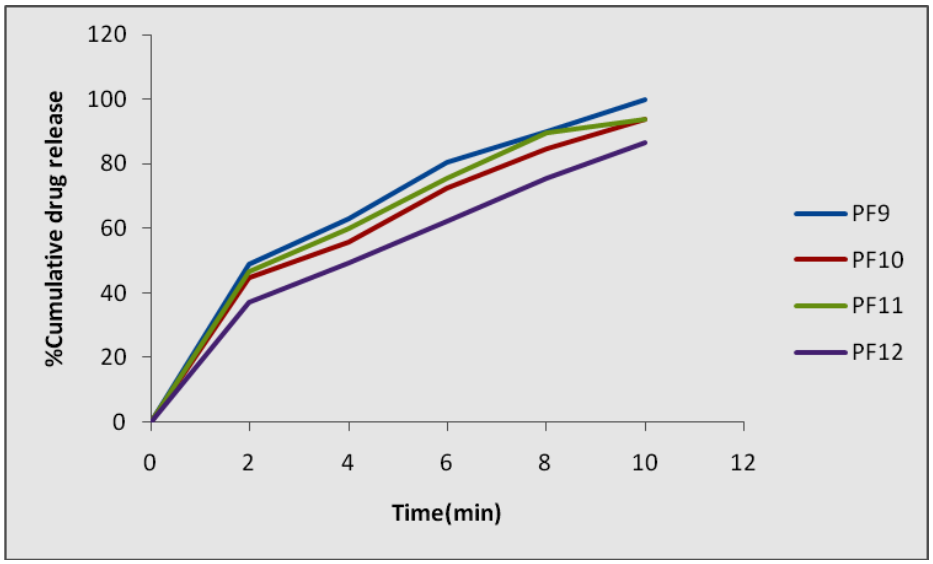

Fig. 4: In vitro drug release profile of Levocetirizine di HCl tablets containing Crospovidone and CCS (PF9-PF12)

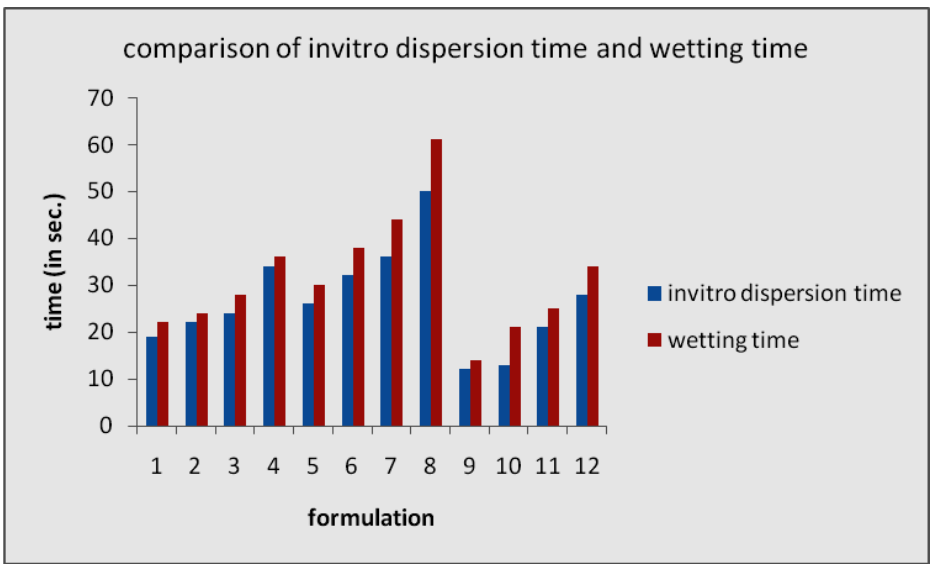

Fig. 5: Comparison of invitro dispersion time and wetting time

RESULTS

The drug- polymer compatibility was confirmed by FTIR studies. The results obtained by FTIR studies revealed that there was no chemical interaction between the pure drug and excipients. The post-compression parameters like the thickness, hardness, friability and *in vitro* dispersion time, wetting time, water absorption ratio and *in vitro* drug release were carried out and the values were found to be within IP, BP limits. The thickness of the batch from PF1-PF12 was found to be 2.436- 2.497mm and hardness was found to be 3.12- 3.69kg/cm^2, The friability of all the formulated tablets of Levocetirizine diHCl was found to be between 0.227-0.376%, All the formulated tablets (PF1-PF12) have shown in vitro dispersion time of less than 60 seconds, Among all the formulations, tablets prepared with crospovidone were shown less than 40 sec. of dispersion time. The wetting time of all the formulations (PF1-PF12) were found to be within 14-61 seconds, The water absorption ratio of all the formulated batches was found to be 85-119 % The drug content of all the nine formulations of Levocetirizine dihydrochloride tablets were found to be within the range of 98.53-100.61%. The formulations PF1, PF5, PF6, PF9, PF10, PF11 containing SSG, SSG and CP, CP and CCS showed more than 90% drug release. Among those six formulations PF9 showed highest drug release of 99.81%. The data for *in vitro* drug release of formulations was shown in Tables, the *in vitro* drug release profiles were shown in Fig.2,3,4.

REFERNCES

1. Pandey S, Shenoy V, Agarwal S, Gupta R. Optimizing fast dissolving dosage form of diclofenac sodium by rapidly disintegrating agents. Ind J Pharm Sci 2003; 23(3):197-201.
2. D. Shukla et al., Mouth Dissolving Tablets I: An Overview of Formulation Technology, Scientia Pharmceutica. 2009; 76; 309–326.
3. Hirani et al., Orally Disintegrating Tablets: A Review, Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 163
4. Shukla D, Chakraborty S, Mouth Dissolving Tablets I: An Overview of Formulation Technology, Sci Pharm. 2009; 76; 309–326.
5. Jaysukh J Hirani1, Dhaval A Rathod, Kantilal R Vadalia, Orally Disintegrating Tablets: A Review, Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 161-172
6. Rangasamy Manivannan Oral disintegrating tablets: a future compaction ijprd/2009/pub/arti/vov-1/issue-10/Dec/005 pg. No 7.
7. Ratnaparkhi Mukesh P, Dr. Mohanta GP, Dr. Upadhyay Lokesh. Review on: Fast dissolving tablet. J Pharmacy Res 2009; 2(1): 5-12.
8. Lachman Leon, Liberman Herbert A, Kanig Joseph L. The Theory and Practice of Industrial Pharmacy. 3rd ed., Varghese publishing house; 1987: 296-303.
9. Rai Rajesh Roshan, Chirra Pavithra, Thanda Venkataramudu. Fast dissolving tablets: A novel approach to drug delivery–A Review. Int J Preclinical and Pharma Res 2012; 3(1): 23-32.
10. Bikshapathi Darna, Saikrishna Kandikonda, Uppuluru Ashok Kumar, Sabitha Gade, Saikumar Bhupathi. Fast dissolving tablets: An update. Int Res J Pharmacy 2011; 2(3): 45 53.
11. Siddiqui N., Garima Garg G., Pramod Kumar Sharma P.K. fast dissolving tablets: preparation, characterization and evaluation: an overview, International Journal of Pharmaceutical Sciences Review and Research, 4(2), 2010; 8.