Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Issue 4, 2012

Research Article

FORMULATION, OPTIMIZATION AND EVALUATION OF FAST DISINTEGRATING TABLET OF MEBEVERINE HCL

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Received: 02 May 2012, Revised and Accepted: 25 Jun 2012

ABSTRACT

Mebeverine HCl is an antispasmodic drug which is widely used in treatment of smooth muscle spasm of the gastrointestinal tract but it undergoes to first pass Metabolism. So that to develop fast disintegrating tablet of Mebeverine HCL to avoid first pass metabolism and increase bioavailability. This offers a new range of product having desired characteristics and intended benefits. In this study, the fast disintegrating tablets were prepared using direct compression method. Tablets produced by direct compression method contain D-Mannitol as diluents, crosscarmellose sodium as a superdisintegrant and sodium saccharine as a sweetener. The dissolution study was performed on PBS 6.8 (salivary pH) and the In-vitro release was found 99.63% without leaving residue for F3 Batch..

Keywords: Mebeverine HCl, Fast disintegrating tablet, Direct compression method.

INTRODUCTION

The concept of Fast disintegrating Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. A Fast disintegrating drug delivery system, in most cases, is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. These are also called melt-in-mouth tablets, repimelts, spongy tablets, orzo-dispersible, quick dissolving or rapid disintegrating tablets. It would, therefore, be advantageous for administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients and who refuse to swallow, such as pediatric, geriatric & psychiatric patients with improved compliance and Good mouth feel property. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of Fast disintegrating Tablet, When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form Fast disintegrating drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple Fast disintegrating OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been noteworthy increases in the number of new chemical entities under development using a Fast disintegrating drug delivery technology. Pharmaceutical marketing and pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form. [1-3]

Various techniques can be used to formulate Fast disintegrating tablets. Direct compression one of the techniques requires the incorporation of a super disintegrates into the formulation the use or highly water soluble excipients to achieve fast tablet disintegration. [14] Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

The aim of purpose work was to formulate and characterization Fast disintegrating tablets of Mebeverine Hydrochloride for rapid dissolution of drug and absorption, which may produce the rapid onset of action in the treatment of smooth muscle spasm of the gastrointestinal tract.

MATERIALS AND METHODS

Mebeverine HCl was procured as a gift sample from United State Vitamin Pharma Ltd, Mumbai (Maharashtra).Microcrystalline cellulose (Avicel PH 102,and Avicel PH101) crosscarmellose sodium (Ac-Di-Sol),was procured as gift sample from Glenmark Pharma Ltd Nashik.&, Crosspovidone (Polyplasdone XL), Sodium Starch Glycolate (Primogel), procured as a gift sample from Gujarat microwax; mannitol, sodium saccharine, Magnesium stearate and Talc are purchased from S.D. Fine Chemicals.

Preparation of Fast Disintegrating tablet [10]

Tablets containing Mebeverine HCl were prepared by direct compression method. Tablets are compressed directly from powder blends of active ingredient and suitable excipients (including fillers, disintegrates, and lubricants). Drug, directly compressible Mannitol, Superdisintegrant (Sodium starch glycolate, Ac-Di-Sol and Crosspovidone), Microcrystalline Cellulose PH 101, sodium saccharine, Vanilla flavor and Talc were mixed together for 20 min. Magnesium stearate, was then added and mixed for 5 min. The powder blend was compressed into the tablets on tablet punching - machine.

Table 1: Composition of different batches of Fast disintegrating tablets of Mebeverine Hydrochloride

Ingredient(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Mebeverine HCL	135	135	135	135	135	135	135	135	135
Crosscarmellose sodium	6	9	12	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	6	9	12	-	-	-
Crosspovidone	-	-	-	-	-	-	6	9	12
MCC(PH 101)	70	67	64	70	67	64	70	67	64
Mannitol	83	83	83	83	83	83	83	83	83
Sodium saccharine	2	2	2	2	2	2	2	2	2
Vanilla	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Mg.Sterate	3	3	3	3	3	3	3	3	3
Talc	1	1	1	1	1	1	1	1	1
Total	300	300	300	300	300	300	300	300	300

Evaluation of tablet[12,13,16,17]

Precompression Parameters

The static angle of repose was measured according to the fixed funnel and free standing cone method. The flowability of the mixed powder was calculated by determining the Hausner's ratio and Carr's index from poured and bulk densities of a known weight of sample using measuring cylinder and following formula Hausner's ratio = Dp ÷ Dt. Carr's Index % = [(Dp–Dt)÷Dp]X 100, where Dp = poured density, Dt = tapped density.

Post Compression Parameter

Evaluation of Fast disintegrating tablet

The formulated tablets were evaluated for different parameters like general characteristic, uniformity of weight, hardness, wetting time, disintegration test and drug release profile.

Weight variation test

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighting balance. The average weight of one tablet was determined from the collective weight. [1,2]

Hardness

Hardness in simple term is the property of material by which it is able to hold all its constituents in an intact form. Hardness is amount of strength of tablet to withstand mechanical shocks of handling in manufacture, packaging and shipping and tablet should be able to withstand reasonable abuse when in the hand of consumer.The hardness of tablet is evaluated by Monsanto hardness tester or Pfizer tester**.** The hardness is measured in kg/cm2.[1,2]

Friability

Friability is also mechanical strength of tablet. It is evaluated by Roche Friabilator with 100 revolution rotating 25 per minute for 4 min by using 6 tablets. According to USP tablets should have limit < 1% for acceptance.

(Wt. of 20 tablets before rotation – Wt. of 20 tablets after rotation) x 100

% Friability = Wt. of 20 tablets before rotation.

Drug content

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder containing about 0.5 g of Mebeverine Hydrochloride, dissolve in 100 ml of 0.1 M hydrochloric acid and heat for 10 minutes on a water-bath, shaking occasionally. Cool, add sufficient 0.1 M hydrochloric acid to produce 250.0 ml and filter. To 10.0 ml of filtrate add sufficient 0.1 M hydrochloric acid to produce 100.0 ml and dilute 10.0 ml of this solution to 100.0 ml with the same solvent. Measure the absorbance of the resulting solution at the maximum at about 263 nm (2.4.7). Calculate the content of C25H35NO5,HCl. Taking 263 as the specific absorbance at 263 nm[4]

Wetting time

Wetting time of the fast disintegrating tablet is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. This method will duplicate the in vivo disintegration, as the tablet is motionless on the tounge. Five circular tissue papers of 10 cm diameter were placed in a Petri dish with a 10cm diameter. Ten millimeters of water containing methyl red, a water-soluble dye, was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as a wetting time. [12,13]

***In vitro* disintegration time**

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 37±0.50C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.[4]

***In vitro* dissolution testing**

Dissolution study was conducted for all the formulation using USP type-II apparatus. The release study was carried out in USP Type 2 dissolution apparatus containing 900ml 6.8 pH phosphate buffers at 50 rpm and 37°C temperature indicated in figure 3,4,5.[18,19]

Table 2: Micromeretic properties of prepared blend of mebeverine HCL

Formulation code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index	Hauser ratio
F1	32.04± 0.22	0.550± 0.28	0.790± 0.34	30.37± 0.18	1.43
F2	33.30± 0.12	0.572± 0.32	0.812± 0.22	29.55± 0.22	1.41
F3	37.08± 0.18	0.562± 0.30	0.849± 0.26	33.80± 0.20	1.51
F4	24.03± 0.20	0.814± 0.22	0.910± 0.24	10.54± 0.24	1.11
F5	26.02± 0.16	0.824± 0.24	0.915± 0.28	9.94± 0.16	1.11
F6	27.80± 0.24	0.852± 0.20	0.932± 0.42	8.58± 0.28	1.09
F7	29.20± 0.18	0.301± 0.26	0.326± 0.38	7.66± 0.24	1.08
F8	30.50± 0.14	0.312± 0.28	0.342± 0.32	8.77± 0.22	1.09
F9	31.20± 0.12	0.320± 0.32	0.350± 0.30	8.57± 0.20	1.09

Table 3: Evaluation parameters of prepared tablets Fast Disintegrating Tablet of Mebeverine Hydrochloride

S. No.	Batch Codes	Weight variation	Hardness (kg/cm2)	% Friability	Average Wetting time (sec)	Average disintegrating time (sec)	% drug content
1	F1	3.10±0.23	2.97±0.035	0.82±0.056	55.05±2.12	43.05±2.12	98.09±0.22
2	F2	2.92±0.20	3.075±0.035	0.87±0.042	49.5±0.70	39.00±1.41	98.25±0.18
3	F3	3.2±0.40	2.85±0.070	0.72±0.028	44.5±0.70	36±1.41	98.71±0.33
4	F4	3.25±0.70	3.17±0.035	0.92±0.021	51.0±1.41	42.5±0.70	97.89±0.48
5	F5	3.34±1.41	3.0±0.141	0.97±0.014	55.0±2.82	44.5±2.12	98.02±0.25
6	F6	3.15±1.4	3.125±0.035	1.5±0.4242	52.0±1.41	42.0±1.41	97.76±1.15
7	F7	3.42±0.021	3.27±0.14	1.45±0.070	47±1.41	37.5±0.70	97.92±0.75
8	F8	3.21±0.035	3.075±0.100	0.76±0.084	49.5±2.12	40.5±0.70	97.92±0.57
9	F9	3.18±0.23	3.125±0.035	0.84±0.028	46.0±1.41	38.0±1.41	98.15±0.43

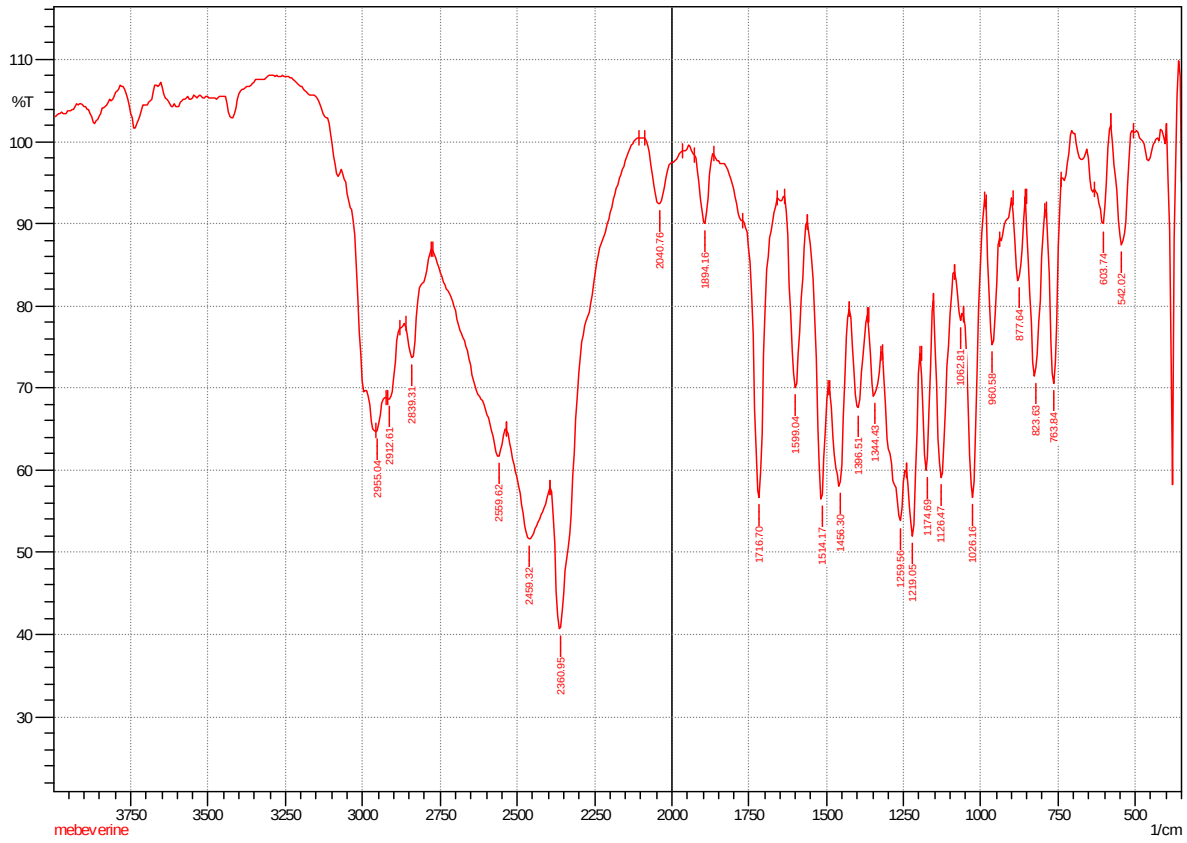

Fig. 1: pure drug IR

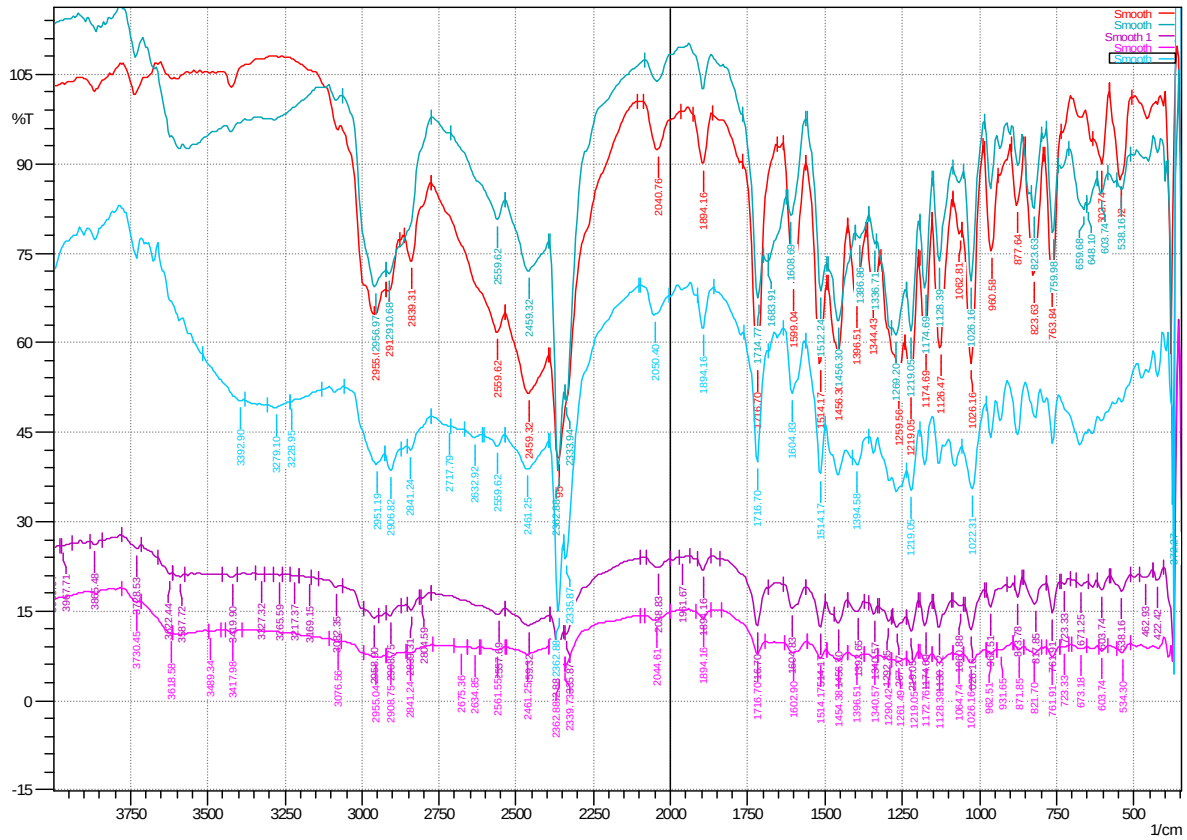

Fig. 2: drug + superdisintegrant IR Overlay

Where, colour indicate Red-Mebeverine HCl, purple- drug+Crosscarmellose sodium, Blue- Drug+Crosspovidone, Pink- Drug+Sodium starch glycolate

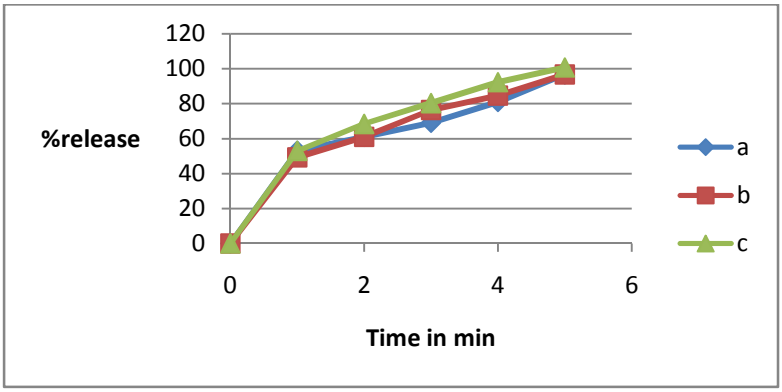

Fig. 3

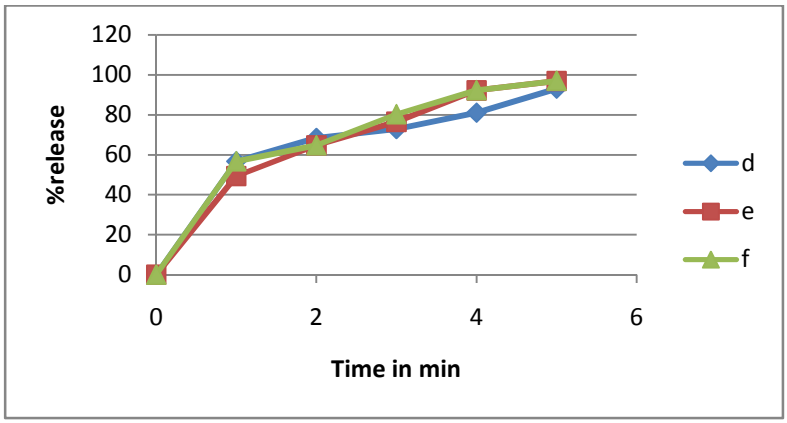

Fig. 4

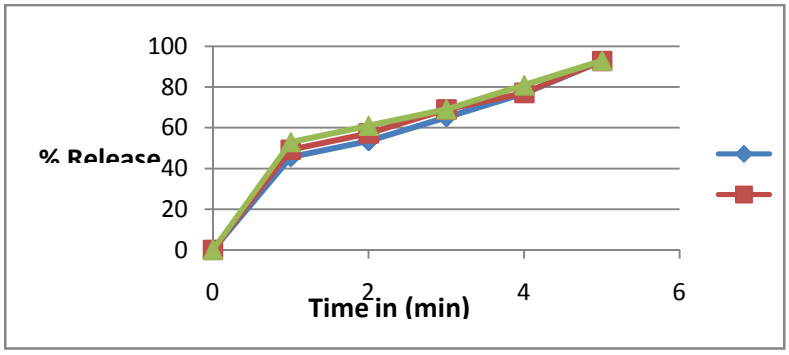

Fig. 5

Fig. 3, 4, 5: Dissolution result, where, a-i batch code 1-9

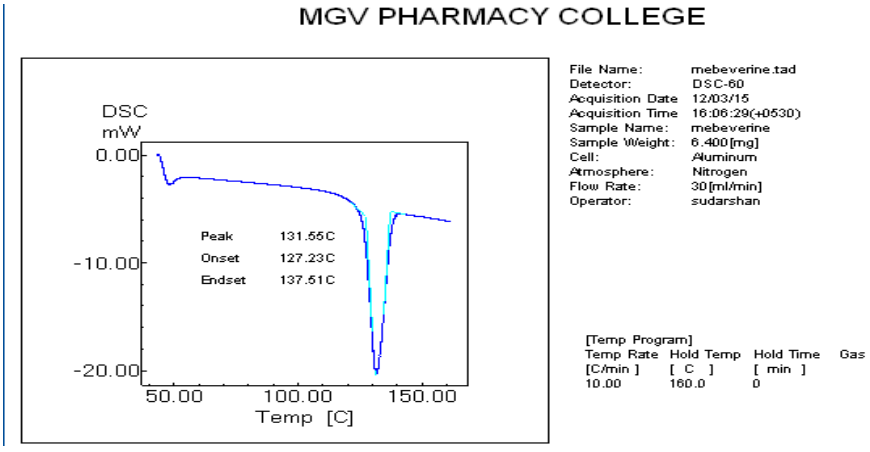

Fig. 6: DSC Thermogram pure drug

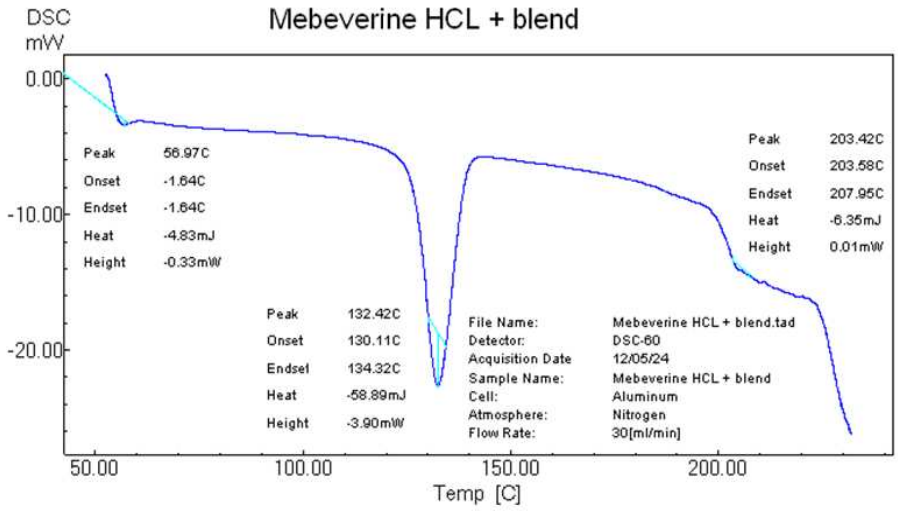

Fig. 7: DSC Thermogram of drug + excipients

RESULTS AND DISCUSSION

Fast disintegrating tablets of Mebeverine Hydrochloride were prepared by super disintegrates addition method and evaluated for various evaluation parameters of the tablets. Total Nine formulations were designed. The hardness of tablets from all formulations was in between 2.80 to 3.25 kg/cm2. All the formulations showed friability below 0.9 %. All the tablets were found to pass the uniformity of weight. Content of Mebeverine Hydrochloride from all formulation was found in range of 96.00% to 99.15%. All the formulations tablets disintegrate in 35 to 50 sec respectively. The wetting time was measured and found in range of 34.50 to 55.00 sec. There is no interaction between drug and excipients as shown in IR(figure 1,2) and DSC Thermogram(figure 6,7).Super disintegrants Crosscarmellose sodium batch no. **F 3** displays best results among nine batch of the Fast disintegrating Tablet. The *in-vitro* release study was carried out using 900 ml of 6.8 pH phosphate buffer as dissolution medium at 50 rpm using USP dissolution apparatus.

Formulation F 3 showed rapid dissolution and cumulative drug release at the end of 5 min. was more than 98% in 6.8 pH phosphate buffer.

ACKNOWLEDGMENT

Authors are highly grateful thanks to company to provide me gift samples and my college to give me all necessary chemicals in the field of research. I highly thankful to my research supervisor, co-supervisor and my parents to provide me necessary guide and support.

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