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Research Article

FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLET OF MEFENAMIC ACID AND DICYCLOMINE HYDROCHLORIDE BY DIRECT COMPRESSION METHOD

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ABSTRACT

Approximately one-third of the patients need quick therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to reduced overall therapy effectiveness. A new dosage format, the immediate release pharmaceutical form has been developed which offers the combined advantages of ease of dosing and convenience of dosing. So there is need to designed Immediate release tablet to release the medicaments with an enhanced rate. Mefenamic acid is a anti inflammatory drug while Dicyclomine HCl is anti cholinergic drug. Combination of Mefenamic acid & Dicyclomine HCl not only controls pain very effectively, but also relaxes bodily spasm which commonly arises from menstruation or intestinal colic spasm. To give the fast relief and quick onset of action than conventional dosage form. For preparation of immediate release tablet nine formulas were designed using 3^2 factorial design in which Crosscarmellose sodium and Crospovidone were used as superdisintegrants in varying concentration. The effects ot types and concentrations of superdisintegrant on the disintegration tiome and dissolution profile of Mefenamic Acid and Dicyclomine HCl Immediate release tablets were studied. The % drug release of Immediate release tablet batch F9 has shows 98.97% of Mefenamic acid and 95.09 % of Dicyclomine HCl after 16 minutes and disintegration time shows in 42 seconds..

Keywords: Mefenamic acid, Dicyclomine HCl, Superdisintegrants, Direct compression method.

INTRODUCTION

Because oral administration of drug is simple, convenient and safe, it is the most frequently used route. At least 90% of drug used to produce systemic effects are administered orally [1-4].

Immediate release tablet

Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. The term "release" includes the provision (or presentation) of drug from the formulation to the gastrointestinal tract, to body tissues and/or into systemic circulation**.** Tablet is the most popular among all dosage forms existing today because of its convenience of self-administration, compactness and easy manufacturing; however in many cases immediate onset of action is required than conventional therapy. To overcome these drawbacks, immediate release pharmaceutical dosage form has emerged as alternative oral dosage forms. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymelhylcellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration.[5-8]

Superdisintegrants

Superdisintegrant are the agents added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule "slugs' into smaller fragments in an aqueous environment there by increasing the available surface area and promoting a more rapid release of the drug substance.[7]

Selection of superdisintegrants

Although superdisintegrants primarily affect the rate of disintegration, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulation should:

- Produce rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
- Be compactable enough to produce less friable tablets.
- Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.

Direct Compression method

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipient 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. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrates, water soluble excipient and effervescent agent. Large and hard tablets have disintegration time more than that usually required. As consequences, products with optimal disintegration properties often have medium to small size and /or high friability and low hardness.[11]

MATERIAL AND METHODS

Materials

Dicyclomine HCl and Mefenamic acid was received as gift sample from Leben Laboratories Pvt Ltd., Akola , Mylan Laboratories Ltd., Nashik, resp., Croscarmellose sodium , Crosspovidone , Micro Crystalline Cellulose, Magnesium Stearate, Talc was received from Modern Science Apparatus Pvt. Ltd., Nashik.

Methods

Drug and Excipients Compatibility Studies

UV spectroscopy

The Mefenamic acid and Dicyclomine HCl drugs were scanned in UV Spectrophotometer to detect the λmax and to drawn the calibration curve of the drug in 0.1N NaOH, 0.1 N HCl as a solvent resp., The drugs were used in concentration ranges of 2-10 ppm for Mefenamic acid and 100-500 ppm for Dicyclomine HCl[1,2] The spectra and calibration curve of both the drugs are as shown in **Figure 1, 2, 3, 4 respectively.**

FTIR spectral studies

The infrared spectra of Mefenamic acid and Dicyclomine HCl were recorded by SHIMADZU 84005 FTIR spectrometer, equipped with an Inferometer detector. Samples were prepared by KBr disc method (2 mg sample in 100 mg KBr) and examined in the transmission mode. Each spectrum was measured over a frequency range of 4000–400 cm−1. The spectra shown in **Figure 5, 6 respectively.**

DSC studies

DSC analysis was performed using Shimadzu-Thermal Analyzer DSC 60 on 2-5mg samples. Sample was heated in an open nitrogen pan at a rate of 10°C/min conducted over a temperature range of 50 to 200°C for Mefenamic acid and Dicyclomine HCl under nitrogen flow of 2 bar pressure. The spectra shown in **Figure 7, 8, 9 respectively.**

Method of Preparation of Powder Blend

For this a 3^2 factorial design was applied using two Excipients (Croscarmellose sodium and Crosspovidone) at three concentration levels. Formulations coded as F1 to F9 respectively. The composition of formula is as shown in **Table 1.** All ingredients were passed through sieve mesh 60#, and blending for 15 mins. Finally the blend was passed through mesh #40 and used for evaluation of flow characteristic.

In- Vitro Evaluation of Powdered Blend[4,5,12,13]

Loose Bulk Density (LBD)

The loose bulk density (LBD) of powder blends was determined using the following formula.

Loose bulk density = Total weight of powder/ Total volume of powder

Tapped bulk density (TBD)

The tapped bulk densities (TBD) of powder blends were determined using the following formula.

Tapped bulk density = Total weight of powder/ Total volume of tapped powder

Hausner's Ratio

Hausner's ratio was determined by following equation.

Hausner's Ratio = tapped bulk density / Loose bulk density

A hausner ratio less than 1.25 indicates good flow while greater than 1.5 indicates poor flow.

Carr's Compressibility Index

The compressibility indices of the powder blends was determined using following formula,

Carr's Compressibility Index (%) = [(TBD - LBD)/ TBD] x100

Angle of repose

The angle of repose, θ was calculated from the following relationship.

$$\tan \theta = h/r$$

Where,

h is height of the pile of powder (h=1) and

r is the radius of the base of cone.

Compression of Powder Blend into Tablet

Immediate release tablet were prepared by direct compression method. Before compression, the surfaces of the die and punch were lubricated with talc. Compression was done by 10-station rotary tablet compression machine (General Machinery Co., Mumbai.) equipped with flat-faced 11 mm punches. Formula is shown in Table 1.

In- Vitro Evaluation of Immediate Release Prepared Tablets

Thickness

The thickness of tablet is important for uniformity of tablet size. The thickness of the tablets was determined using a VernierCalliper.

Hardness

For each formulation, the hardness of three tablets was checked using the Monsanto hardness tester (LAB- HOSP).

Drug Content Uniformity Study[3]

Twenty tablets were weighed accurately an d crushed into a fine powder. Powder equivalent to 100mg of MefenamicAcid. was weighed accurately and transferred into a 100 mL volumetric flask with 60 ml 0.1 N HCl. The content was shaken for 15-20 min, diluted to volume with 0.1 N HCl, and filtered using a Whatman No. 42 filter paper. First 10 mL port ion of filtrate was discarded and subsequent portions were subjected to analysis. Results are reported in **Table 3.1 and 3.2.**

Friability Test

Friability is the measure of tablet strength. In this test number of tablets subjected to combined effect of shock abrasion by utilising a plastic chamber which revolves at a speed of 25rpm, dropping the tablets at a distance of 6 inches in each revolution. A sample of preweighed tablets was placed in Roche Friability tester (Kumar Mfg. Ltd.) Permitted friability limit is 1.0%[12,13]. Tablets were then weighed and friability values were determined and are reported in **Table 3.1 and 3.2.**

$$\text{Friability} = \frac{W_1 - W_2}{W_1} \times 100$$

Where, W_1 = weight of the tablets before test,

W2 = weight of the tablets after test

Weight variation

Twenty tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the acceptable limits (±7.5%)[12,13]. The percent deviation was calculated using the following formula.

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

Wetting time

A piece of tissue paper folded double was placed in a petridish containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in sec. The method was slightly modified by maintaining water at 37^{0}C. Wetting time corresponding to the time taken for the tablet to disintegrate when kept motionless on the tongue was calculated[12,13]. The result are shown in **Figure 10 &Table 3.1 and 3.2.**

Water absorption ratio

A piece of tissue paper folded twice was placed in small Petri dish (6.5cm) containing 5 ml water. A tablet was put on the tissue paper and allows wetting completely. The wetted tablet was then weighed. The water absorption ratio R was determined using following equation.

$$R = \frac{W_a - W_b}{W_a} \times 100$$

Where;

W_a = weight of a tablet after absorption

W_b = weight of a table before absorption

The result are shown in **Table 3**

Disintegration time study

The *in-vitro* disintegration studies were carried out using Tablet Disintegration Test Apparatus. One tablet was placed in each of the six tubes of the basket assembly and disk was added to each tube. This assembly was then suspended in one-liter beaker containing water maintained at 37±2^{0}C. The basket was then moved up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minutes. The time required for complete disintegration of the tablet was recorded. The test was performed for tablets of all type of formulation (F1-F9).The result are shown in **Table 3.1 and 3.2.**

***In - vitro* Drug Release Study[1,2]**

An *in-vitro* drug release studies of the prepared nine formulations of Immediate release tablets were conducted for a period of 16 minutes using an eight station USP type 2 apparatus (paddle type) (LABINDIA-DISOTEST, 6 F 622). The agitation speed was 50 rpm. Prepared Immediate release tablets were added to 900 ml of phosphate buffer 6.8 at 37 ± 0.5° C and stirred at 50 rpm .5 ml aliquots were withdrawn at time intervals of 2,4,6,8,10,12,14,14,16,18 min. and filtered through Whatmans No. 41 filter paper. An equal volume of fresh dissolution medium was replaced to maintain the volume of dissolution medium. The filtered samples were analyzed at zero crossing point of respected drugs. Cumulative percentage of labelled amount of drug released was calculated. The result are shown in **Table 4 and 5**

RESULT AND DISCUSSION

The prepared immediate realese tablets were evaluated for thickness, weight variation, hardness, friability, drug content, weight variation, weight absorption and *in-vitro* drug dissolution studies. All the studies were performed in triplicate, and results are expressed as mean ± SD.

Drug and Excipients Compatibility Studies

UV Spectroscopy

The λmax of Mefenamic acid and Dicyclomine HCl obtained at 284.8 nm, 213 nm respectively and the calibration curve was constructed using concentration range 2-10 ppm, 100- 500 ppm respectively equation was found to be y = 0.043X + 0.01,y =0.005 X + 0.090 respectively and the regression coefficient R^2 = 0.998, R^2= 0.993 respectively. Spectra and calibration curve showed **Figure 1, 2, 3, 4.**

FTIR spectral studies

FTIR spectra of Mefenamic acid, Dicyclomine HCl and the optimized formulations are shown in **Figures 5, 6.** The FTIR spectrum of Mefenamic acid exhibited at 756.12 cm^{-1} (Aromatic C=C vibration), 31161.19 cm^{-1} (Aromatic O-CH bond), 1257.64 cm^{-1} (bending of O-H bond), 1577.82 cm^{-1} (stretching for C=O), and 1651.12 cm^{-1} (N-H Stretching). FTIR spectrum of Dicyclomine HCl exhibited at 1136.11 cm^{-1} (C- N stretching), 1195.91 cm^{-1} (C- O stretching), 1720.56 cm^{-1} (C=O [ester] Stretching) and 2935.76 cm^{-1} (C-H Stretching). All these characteristic bands were all retained in formulations indicating that there is no interaction between drug and polymers.

DSC analysis of pure drugs

DSC Thermograms of Mefenamic acid, Dicyclomine HCl and were shown in **Figures 7and 8.** Mefenamic acid showed sharp endothermic peak at 229.79°C corresponding to its melting point. While Dicyclomine HCl showed sharp endothermic peak at 167.97°C corresponding to its melting point.. Overall DSC curves indicate that there is no interaction observed between drug and excipients.

DSC study of immediate release formulation

The DSC curve of Mefenamic acid and Dicyclomine HCl tablet shows sharp endothermic peak at 242.7°C and 168.30°C respectively. The drug do not undergoes decomposition following its melting. This indicating that there is no probable chemical interaction between drug and excipients mixture. Thermograms is as shown in **Figure 9.**

Pre compressional parameters

The powder blends was prepared by mixing of various ingredients mentioned in **Table 1** and used for characterization of various flow properties of powder. Table 2 reports the values for Compressibility Index (CI) and Hausner's ratio (HR) for all prepared batches. According to the literature, powders with CI values between % -% are suitable for producing the tablets and those with a Hausner's ratio values below 1.25 and angle of repose values in between 20-40˚ indicate good flow properties of powders.The results are shown in **Table2.**

Formulation and evaluation of bilayer tablet

Immediate release tablets were evaluated for hardness, thickness, uniformity of weight,

friability, contents of active matter, weight variation, weight absorption and disintegration time as procedure mention in method. The results are shown in **Table 3.1 and 3.2.**

In-*vitro* dissolution studies

All tests of immediate release tablet are within limit and drug release profile was found to be 98.97 % and 96.99 % in 16 min of Mefenamic acid and Dicyclomine hydrochloride respectively.

CONCLUSION

Approximately one-third of the patients need quick therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to reduced overall therapy effectiveness. A new dosage form, the immediate release pharmaceutical form has been developed which offers the combined advantages of ease of dosing and convenience of dosing. These tablets are designed to release the medicaments with an enhanced rate. Mefenamic acid and Dicyclomine HCl combination therapy is widely used in market. This combination not only controls pain very effectively but also reduce bodily spasm which commonly arises from menstruation or colic spasm. In market the conventional doage form of Mefenamic acid and Dicyclomine HCl is available but it gives slow onset of action. In present study the Immediate release tablet of Mefenamic acid and Dicyclomine HCl were prepared by direct compression method using Crospovidone and Croscarmellose sodium as superdisintegrants. Mefenamic acid and Dicyclomine HCl was initially characterized for its preliminary studies such as organoleptic properties, melting point, solubility, UV Spectroscopy and FTIR studies and also drug-excipients compatibility was confirmed by FTIR.

Optimization of Immediate release tablet was carried out by *in vitro* drug release at 16 min., disintegration time. The nine formulations prepared were subjected to physical evaluation parameters like hardness, thickness, weight uniformity, wetting time, drug content uniformity, Water absorption ratio, *in vitro* drug release, disintegration time.

The conclusion of the research project is as follows:

- The Mefenamic acid showed λ_{max} at 285 nm in 0.1N NaOH, 284.8nm in 6.8 pH phosphate bufferand its melting point was fond to be 228-229 ^{0} C.
- The Dicyclomine HCl showed λ_{max} at 212.8 nm in 0.1N HCl, 213 nm in 6.8 pH phosphate buffer and its melting point was fond to be 169-171^{0} C.
- The peaks observed in IR spectrum of both drug were also seen in the drug-excipients mixture; hence leading to conclusion that drugs was compatible with all the excipients. The DSC studies also concluded that drug was compatible with all the excipients
- All tablets prepared, were uniform in thickness, hardness, drug content,weight variation and they also show good % drug release. F9 batch shows good % drug release in 16 minutes, disintegration time is 42 second, wetting time is 37 second.
- Thus Immediate release tablet of Mefenamic acid and Dicyclomine HCl F9 batch was optimized.

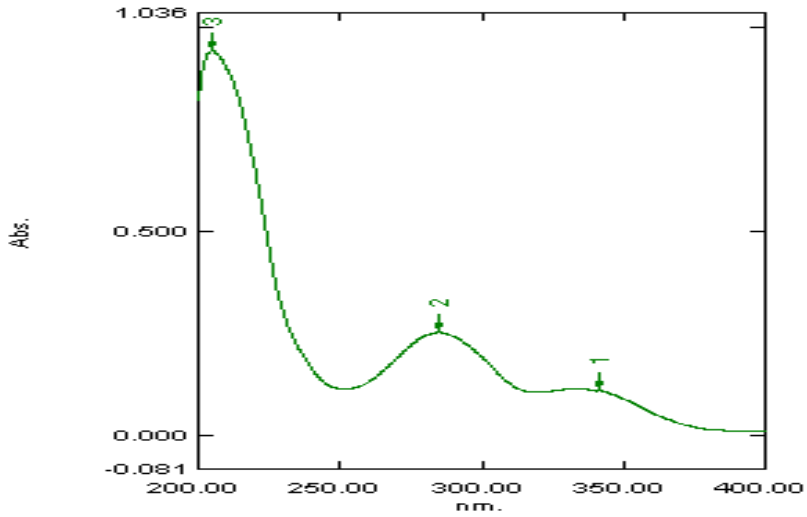

Fig. 1: UV Spectrum of Mefenamic Acid in 0.1 N NaOH of 10 ppm

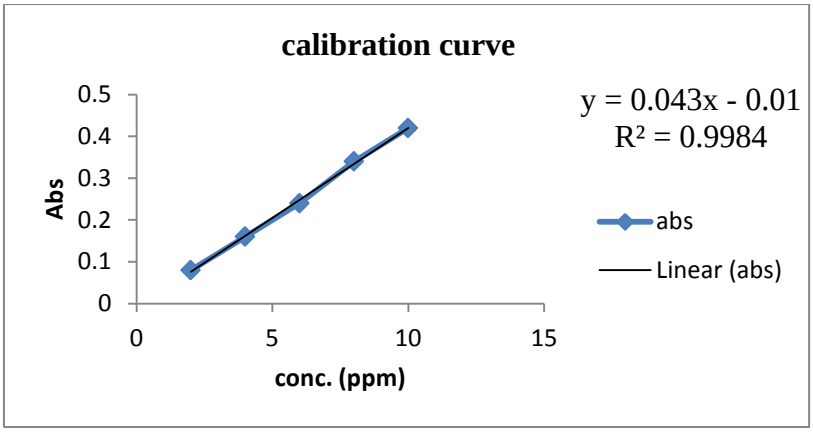

Fig. 2: Calibration Curve of Mefenamic Acidin 0.1 N NaOH

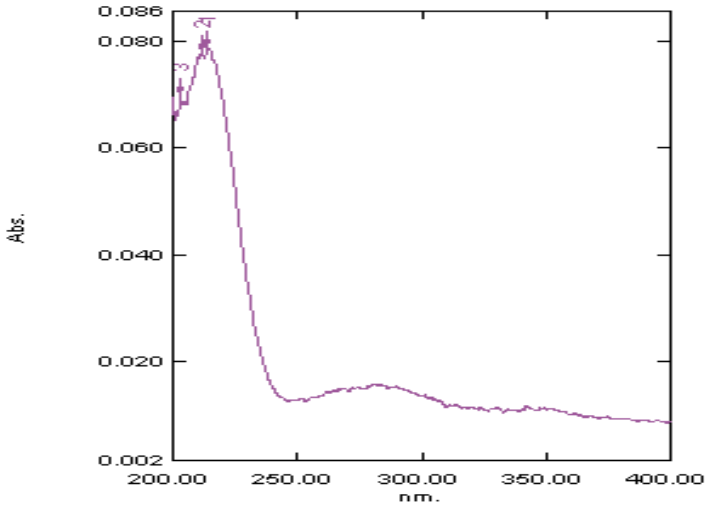

Fig. 3: UV Spectrum of Dicyclomine HCl in 0.1 N HCl of 100 ppm

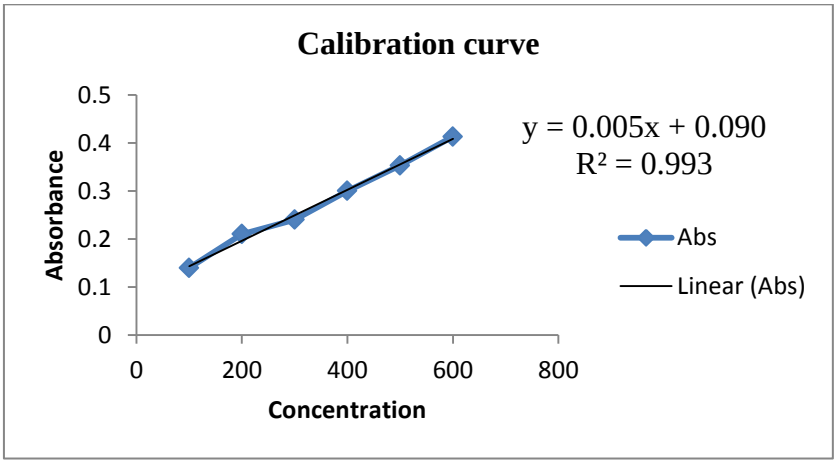

Fig. 4: Calibration Curve of Dicyclomine HCl in 0.1 N HCl

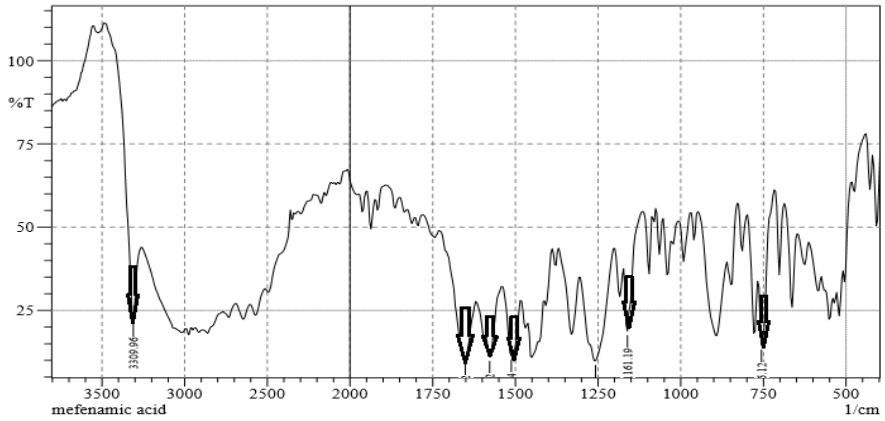

Fig. 5: FT-IR Spectrum of Mefenamic Acid

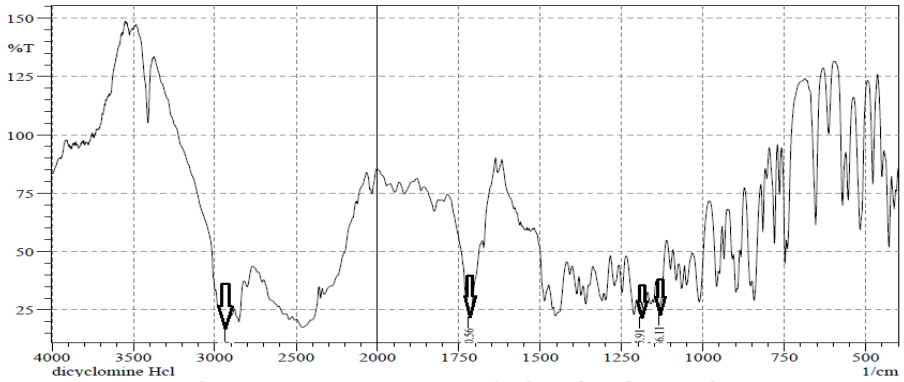

Fig. 6: FT-IR Spectrum of Dicyclomine HCl

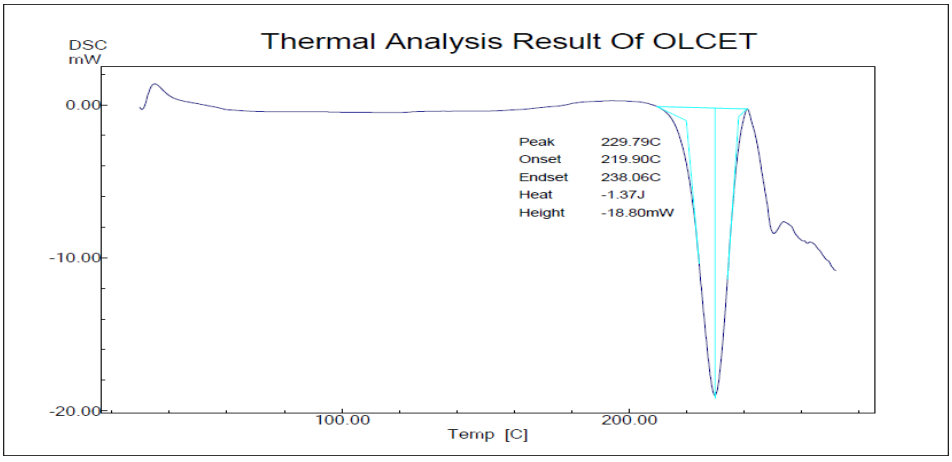

Fig. 7: DSC study of Mefenamic Acid

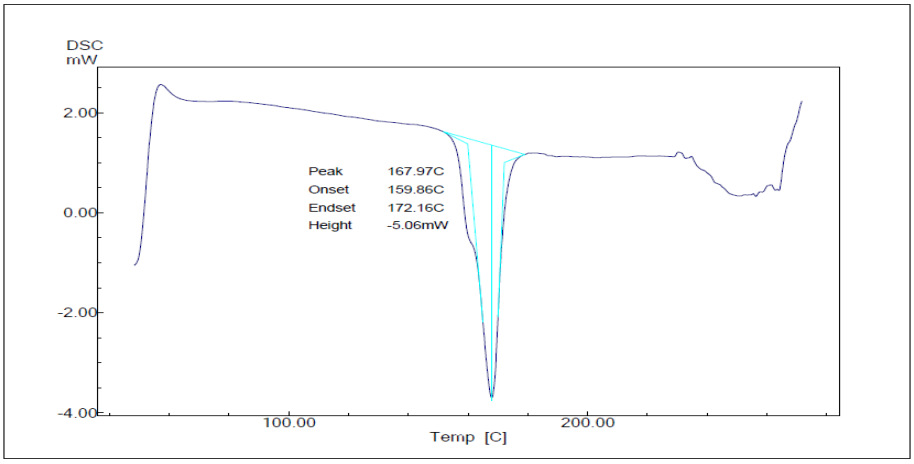

Fig. 8: DSC study of Dicyclomine HCl

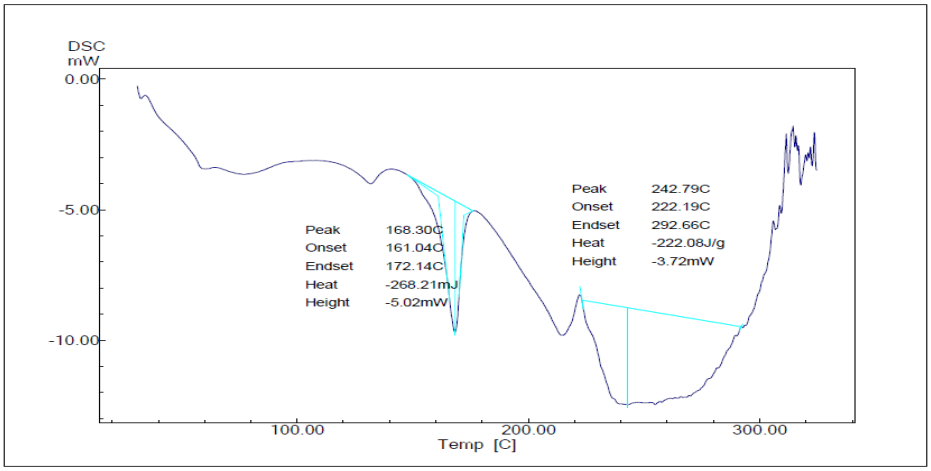

Fig. 9: DSC study drug with physical mixture

Table 1: Formula for Immediate release tablet of Mefenamic Acid and Dicyclomine HCl

Batches Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Mefenamic acid (mg)	250	250	250	250	250	250	250	250	250
Dicyclomine HCl (mg)	10	10	10	10	10	10	10	10	10
CCS (mg)	5.4	9	2.2	5.4	5.4	9	2.2	2.2	9
Crosspovidone (mg)	9	4.5	9	6.75	4.5	6.75	6.75	4.5	9
Talc(mg)	9	9	9	9	9	9	9	9	9
Magnesium stearate (mg)	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Avicel (mg)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Table 2: Evaluation of powder blend containing drug and Excipients

Formulation batches	F1	F2	F3	F4	F5	F6	F7	F8	F9
Loose bulk density	0.418	0.425	0.415	0.398	0.397	0.426	0.421	0.427	0.432
Tapped bulk density	0.483	0.442	0.485	0.461	0.458	0.483	0.480	0.484	0.494
Hausner's Ratio	1.15	1.11	1.16	1.15	1.15	1.13	1.15	1.13	1.14
Compressibility Index (%)	13.45	13.8	14.43	13.66	13.31	13.3	13.7	12.7	13.55
Angle of repose (ɵ)	30.22	32.84	25.30	27.82	32.61	33.12	27.18	26.67	29.35

Table 3.1: Evaluation Parameters of Immediate release Tablets

Formul-ation batches	Parameters				
	Thickness (mm)±SD (n=3)	Hardness (Kg/cm^2) (± SD) (n=3)	% Drug content of MA (± SD) (n=3)	%Drug content of DIC(± SD) (n=3)	Friability (%) (± SD) (n=30)
F1	4.75±0.041	4.87±0.013	96.79 ±1.21	96.49.±1.16	0.65±0.021
F2	4.87±0.019	5.54±0.009	98.13 ±0.54	94.54±1.42	0.51±0.061
F3	4.78±0.08	4.97±0.021	96.45 ±0.87	96.02±1.53	0.56±0.016
F4	4.34±0.027	5.34±0.034	97.76 ±0.80	95.91±1.21	0.47±0.038
F5	4.65±0.039	5.65±0.023	98.67 ±0.67	94.88±1.25	0.54±0.031
F6	4.30±0.030	5.60±0.024	97.59±1.12	94.67±1.53	0.58±0.043
F7	4.12±0.036	5.49±0.031	98.24 ±0.74	95.06±1.78	0.69±0.039
F8	4.32±0.048	4.86±0.019	96.24 ±0.45	95.76±1.41	0.63±0.057
F9	4.89±0.017	5.57±0.021	98.19 ±1.06	96.21±1.36	0.57±0.048

Table 3.2: Evaluation Parameters of Immediate release Tablets

Formul-ation batches	Parameters			
	Weight variation (± SD)(n=20)	Wetting time (sec.)(± SD) (n=3)	Water absorption ratio (%) (± SD)(n=3)	Disintegration Time (sec.)(± SD) (n=3)
F1	0.443±0.067	38±2.08	77.72± 1.99	47±2.51
F2	0.442±0.085	48±1.57	74.22 ±0.58	68±2.67
F3	0.446±0.15	39±1.64	79.59± 1.01	58±1.78
F4	0.440±0.085	46±1.67	76.69 ±1.03	64±2.32
F5	0.444±0.078	51±2.45	69.38± 1.10	70±2.12
F6	0.443±0.12	42±2.67	67.27± 1.73	54±1.96
F7	0.438±0.06	55±1.87	75.73± 1.45	69±2.89
F8	0.441±0.046	59±2.34	65.04 ±1.12	77±1.45
F9	0.446±0.07	37±2.12	75.74 ±2.50	42±2.93

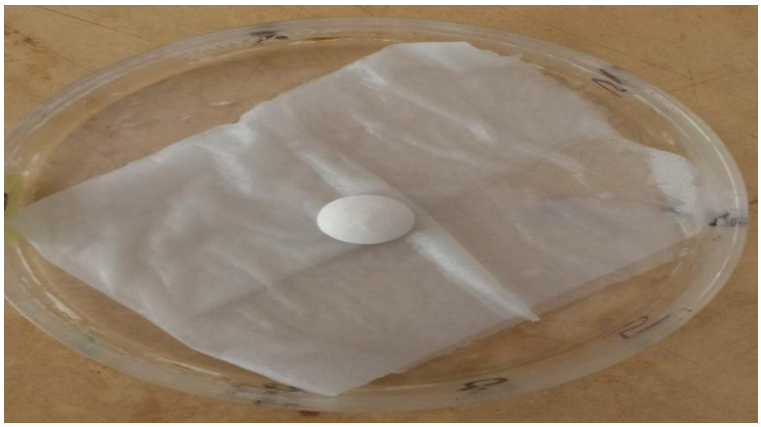

Fig. 10: Wetting time determination of Immediate release tablet

Table 4: *In-vitro* drug Release Study of Mefenamic Acid

Time (min)	% Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	37.67	33.12	33.42	33.91	22.53	34.71	23.83	19.89	38.63
4	48.53	44.42	42.36	44.18	26.18	43.48	35.19	26.69	49.84
6	57.76	56.66	50.19	58.60	36.41	55.29	42.44	34.48	60.01
8	71.32	69.96	61.87	69.50	47.26	68.09	54.84	44.23	72.65
10	82.53	79.71	73.38	77.16	59.24	79.47	63.07	55.65	84.43
12	91.75	84.00	85.57	83.46	69.29	89.98	69.68	64.26	95.15
14	97.23	89.24	89.46	87.56	78.97	95.13	77.47	70.69	98.46
16	98.00	91.84	95.29	90.35	81.74	96.39	83.87	78.45	98.97

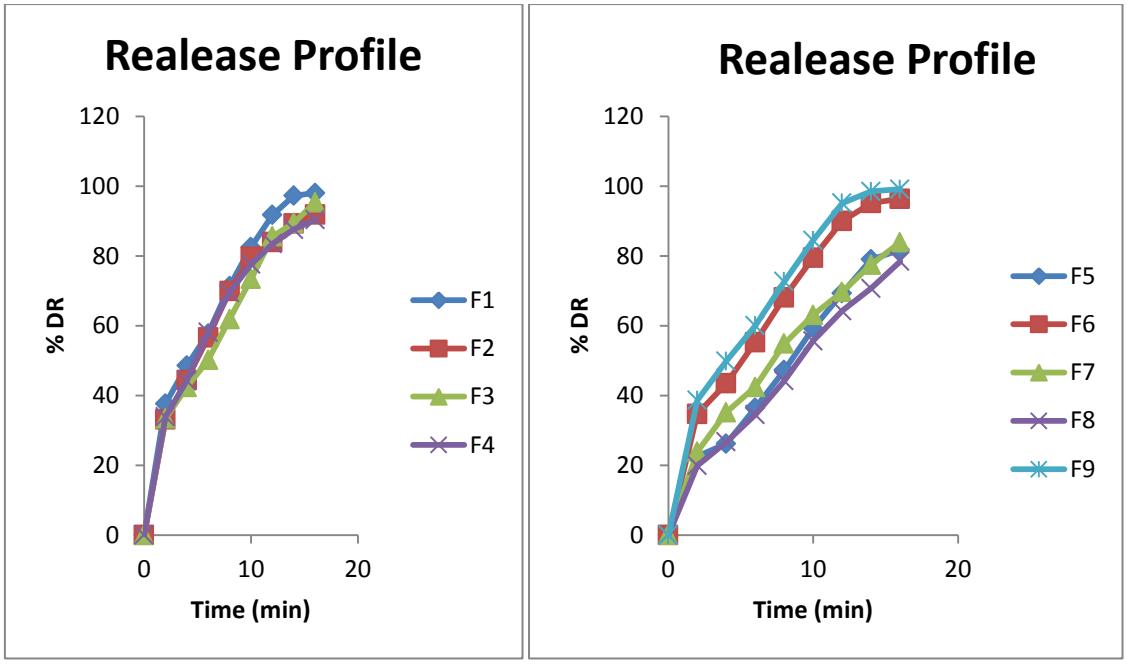

Fig. 11: Dissolution profile of immediate release tablets of Mefenamic Acid

Table 5: *In-vitro* drug Release Study of Dicyclomine HCl

Time (min)	% Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	24.75	21.3	23.85	22.5	22.53	23.4	13.5	11.7	27
4	36.6	26.89	29.85	27.25	28.18	28.48	18.07	14.01	39.15
6	49.86	38.53	39.89	36.27	38.41	38.08	27.17	36.14	54.4
8	61.38	45.2	52.26	49.97	51.26	51.34	36.32	43.09	63.7
10	77.47	58.56	66.05	63.75	64.24	65.13	50.02	50.08	79.35
12	86.9	68.9	75.86	73.1	73.29	74.48	59.3	59.35	89.23
14	91.87	76.25	82.58	78	81.97	82.54	73.12	66.88	96.47
16	93.72	82.23	91.13	85.62	87.74	88.39	82.52	73.54	96.99

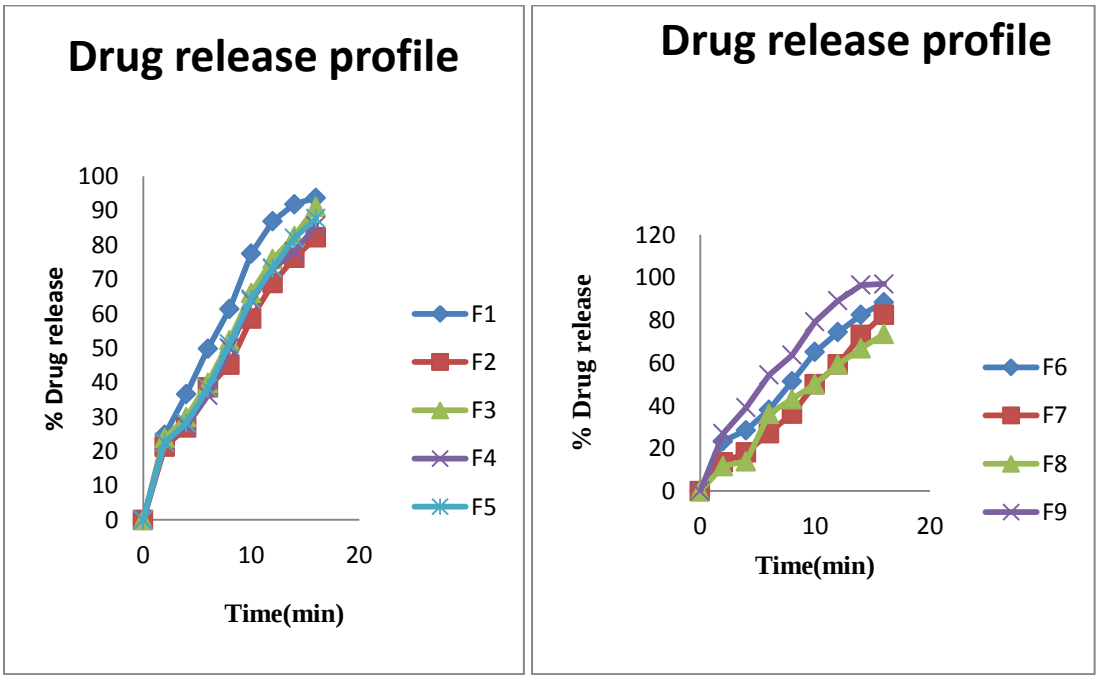

Fig. 12: Dissolution profile of immediate release tablets of Dicyclomine HCl.

Table 6: Result of optimised F9 batch

Parameters	Immediate release tablet (F9 batch)
Organoleptic properties	White
Thickness	4.89±0.017
Hardness	5.57±0.021
Friability (%)	0.57±0.048
Content uniformity (%) for Mefenamic Acid	98.19±1.46
Content uniformity (%) for Dicyclomine HCl	96.21±1.36
Disintegration time (sec)	42±2.93
Wetting time (sec.)	37±2.12
In vitro drug release (%) for Mefenamic Acid	98.97% in 16 min
In vitro drug release (%) for Dicyclomine HCl	95.09% in 16 min

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REFERENCES

1. Panikumar D Anumolu and Gurrala S. Development of Dissolution Test Method for Drotaverine Hydrochloride/Mefenamic Acid Combination Using Derivative Spectrophotometry. Tropical Journal of Pharmaceutical Research. 2013;12(2): 227-232.
2. Roosewelt C and Harihrishnan N. Simultaneous Estimation of DrotaverineHCl and Mefenamic Acid in Tablet Dosage Form Using Spectrophotometric Method. Asian Journal of Chemistry. 2010;22 (2):843-849.
3. Harinder S and Rajnish Kumar. Development of UV Spectrophotometric Method For E stimation Of Mefenamic Acid In Bulk A nd Pharmaceutical Dosage Forms. International Journal of Pharmacy and Pharmaceutical Sciences. 2011;3(2):237-238.
4. Dutt. K and Sharma SK. Immediate Drug Release Tablets: A Review. Advanced research in pharmaceuticals and biological.2014; 4(1):566-570.
5. Rathod VG and Kadam V. Immediate Release Drug Delivery System: A Review. World Journal of Pharmacy and Pharmaceutical Sciences. 2014;3(6):545-558.
6. Jaimini M. and Ranga S. A Review on Immediate Release Drug Delivery System by using design of experiment. Journal of Drug Discovery and Therapeutics. 2013;1(12):21-27.
7. Bhandari N, Kumar A and Choudhary A. A Review on Immediate Release Drug Delivery System. International Research, Journal of Pharmaceutical and Applied Sciences. 2014; 4(1):78-87.
8. Nyol S and Gupta M. Immediate Drug Release Dosage Form: A Review. Journal of Drug Discovery and Therapeutics. 2013;3(2):155-161.
9. Pradeep P and Vasanth PM. Formulation, Development & evaluation of combined Efavirenz & Lamivudine Immediate release tablet-A combination therapy. International research journal of pharmacy.2013; 4(3):145-148
10. Nisarg Patel and Dr.Naruka PS. Formulation, Development & evaluation of Immediate release tablet of Topiramate antiepileptic drug. JPSBR. 2013;3(2): 58-60.
11. Wagh MA, Kothawade PD and Salunke KS. Techniques Used in Orally Disintegrating Drug Delivery System: A Review. International Journal of Drug Delivery. 2010;2:98-107.
12. Bhavsar B and Chauhan M. Formulation, Development & evaluation of Immediate release bilayer tablet of Telmisartan & Hydrochlorothizide. International research journal of pharmacy. 2013;4(9):117-122.
13. Tiwari AK and Shah H. Formulation and in vitro evaluation of immediate release tablet of drotaverine hcl. Journal of chemistry and pharmaceutical research. 2011;3(4):331-341.

14. Sumathi M and Rithika S. Design and evaluation of fast dissolving tablet of mefenamic acid. Internationa Journal of chemistry and pharmaceutical science.2014;5(3):122-125.
15. Singh SK and Mishra D. Fast Disintegrating Combination Tablets Of Omeprazole And Domperidone. Asian Journal of Pharmaceutical and Clinical Research. 2009; 2(3):74-82.
16. Bansal M and Bansal S. Formulation and Evaluation of Immediate Release Tablets of Zaltoprofen. Scholars Academic Journal of Pharmacy. 2013;2(5):398-405.
17. Raghavendra Rao NG and Venkatesh K. Design and development of fast dissolving tablets containing baclofen by direct compression method. International Journal Of Pharmaceutical And Biomedical Research. 2012;3(4): 216-221.
18. Rowe R, Sheskey PJ and Weller PJ. Hand book of pharmaceutical excipient , edited by K.M. Varghese Publication. 2003;4th Edn:206-208,404,728.
19. Brahmankar DM and Jaiswal SB. Biopharmaceutics and Pharmacokinetics -A Treatise, edited by Vallabh Prakashan, New Delhi. 2011;2nd Edn: 431-450
20. The-Merkindex-An encyclopedia of chemicals,drugs,&biological, Published by Merck research laboratories of division of merck and cooperation. NJ. 2001;13th Edn: 3125,1036