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DEVELOPMENT AND EVALUATION OF FAST DISPERSIBLE KETOPROFEN 100mg TABLETS

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ABSTRACT

The aim of this study is to develop fast dispersible Ketoprofen 100mg tablets using direct compression technique. Nine different formulations were investigated using Ludipress as filler in the range of 12-48 % and Ac-di-sol as superdisintegrantin the range of 0.1-4%. Powder blends of all the formulations were tested for the determination of flow properties including Carr's index, Hausner's ratio and Angle of Repose. Different physico-chemical parameters including thickness, diameter, hardness, friability, weight variation, disintegration, dissolution and assay were performed and the results were found in the acceptable limits. F-6 was selected as the best formulation on the basis of shortest disintegration time 19 sec, 99.26 $\pm$ 0.94 % dissolution and tablet weight i.e. 122.34 $\pm$ 1.08 mg. Profiles comparisons were done in 0.1N HCL, phosphate buffer pH 4.5 and pH 6.8. Data were evaluated by model dependent and model- independent methods. The best formulation was found to be F-6 in 0.1N HCl having r^2=0.978 in first order, r^2=0.992 in Higuchi andr^2=0.969 in Hixson-Crowell model and F-5 in phosphate buffer pH 4.5having r^2=0.993 in first order, r^2=0.991 in Higuchi and r^2=0.990 in Hixson-Crowell model. F-6 and immediate release (core tablet) were taken as reference formulations for the determination of $f_2$similarity factor. Results indicated that all the formulations were similar to the F-6 and immediate release (Reference) formulation in different dissolution media.

Key words: Ketoprofen, Fast dispersible, Direct compression, Model dependent, Model- independent.

INTRODUCTION

Ketoprofen [2-(3-benzoylphenyl) propionic acid] is a non-steroidal anti-inflammatory and analgesic compound listed among the mainly effective inhibitors of the cyclo-oxygenase path of the arachidonic acid cascade, and inhibits lipo-oxygenase[1]exerting analgesic and antipyretic actions [1,2]. Ketoprofen is also used for acute and chronic rheumatoid arthritis and osteo-arthritis [3]. Therefore, fast dispersible formulation of Ketoprofen will produce its impact on patients of all age groups. Water dispersible tablet is defined as dosage form when disperse in water, quickly forms a suspension [4]. Dispersible tablets are of two different types from which one type of dispersible tablet disintegrates very rapidly in the mouth after swallowing, without the use of drinking water. While the other type offers rapid dispersion in water which can be easily swallowed by the patients [5]. The advantages of dispersible tablets are numerous which are accepted by the manufacturers and patients which includes it's convenient utilization by the patient, distinctive way of taking tablets and reduced the risk of first-pass effects [6]. Due to these advantages these types of dosage forms have gained the interest of many formulators [7]. Freeze drying, moulding and direct compression techniques are mainly used to manufacture this type of dosage form [8,9]. Direct compression method offers various advantages which include fewer manufacturing steps, complete withdrawal of heat and moisture, enhanced productivity and decrease in the final cost of the product. Researchers also found that this method is used for hygroscopic and heat sensitive compounds [10,11]. In order to formulate fast dispersible tablets it is very important to select appropriate excipients

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fine compaction and disintegration ability. Factors including tablet hardness and friability must be considered when choosing a superdisintegrant for the formulation [12]. The presence of disintegrants having high swelling and disintegrating property was claimed as an important parameter for rapid dispersion of tablet in water [13]. The aim of this study was to develop cost effective fast dispersible tablets containing Ketoprofen as a model drug. In the present study different formulations were developed using direct compression method. All the formulations are evaluated by different physico-chemical tests. After in vitro dissolution profiles comparison in 0.1N HCl, phosphate buffer pH 4.5 and pH 6.8, data were analysed by model - independent and model dependent methods using first order, Higuchi kinetics, Hixson –Crowell cube root law and Weibull model.

EXPERIMENTAL

Materials

Ketoprofen ($C_{16}H_{14}O_3$) Ac-di-sol, Aspartame were donated by Aventis Pharma (Pvt.) Ltd and Ludipress (BASF, Ludwigshafen, Germany) were used as directly compressible excipients in the present study.

Methods

Preparation of Fast Dispersible Tablets

Formulations (F1-F9) of Fast Dispersible Ketoprofen tablets were prepared by direct compression method having Ketoprofen 100mg, Aspartame (0.82-1.39%), Ludipress (12-48 %) and Ac-di-sol (0.1-4%) were accurately weighed (Mettler Toledo, Switzerland) and passed through 20-mesh sieve size. Powder blends of all the formulations were then mixed by tumbling action. At the end, powder blends were compressed with single punch tablet machine (Korsch Erweka, Frankfurt Germany) as shown in table 1.

Evaluation of Blends

The powder blends were tested for the determination of flow properties as given below:

Compressibility (Carr Index) and Hausner's ratio

In order to determine the flowability of powder, ratio of tapped density and bulk density can be expressed in the following two ways [14].

$$\text{Hausner's ratio} = \frac{\text{tapped density}}{\text{bulk density}} \quad (1)$$

$$Compressibility Index = 100 \times \left(\frac{Tappedbulkdensity - Pouredbulkdensity}{Tappedbulkdensity}\right) \quad (2)$$

Bulk and Tapped densities

A known amount of powder blend was filled in a 100ml graduated cylinder. The volume of the blend was then read from the cylinder in order to determine the bulk density. For the evaluation of tapped density, the graduated cylinder was tapped 100 times [15].

Where:

$$\text{Poured bulk density} = \frac{\text{powder mass}}{\text{bulk volume}} \quad (3)$$

$$\text{Tapped bulk density} = \frac{\text{powder mass}}{\text{tapped volume}} \quad (4)$$

Angle of Repose

The angel of repose was determined by funnel method. In order to obtain the maximum cone height, powder blend was poured through a funnel [15], from the heap height and radius of the heap, angle of repose was determined as follows:

$$\theta = \tan^{-1}\frac{h}{r} \quad (5)$$

Evaluation of Fast Dispersible Tablets

Tablets were examined by various physical parameters including hardness test (OSK Fujiwara, Ogawa Seiki Co. Ltd., Tokyo, Japan), thickness and diameter test were evaluated by vernier caliper, weight variation test (Mettler Toledo B204-S, Switzerland) and friability test (H.Jurgens GmbH and Co., Bremen, Germany) were done according to the British Pharmacopoeia [16] .

Disintegration test for Dispersible Tablets

For dispersible tablet maximum disintegration time is 3 minutes. The disintegration test was performed in water at 15^0C to 25^0C using USP <701> Basket Rack Assembly [17].

Test for finess of Dispersion

For the determination of finess of dispersion, place two tablets in a beaker containing 100ml of water and stir gently until both the tablets are dispersed. Pass this dispersion through a sieve having 710µm mesh aperture.

Pharmaceutical Assay

Twenty tablets were weighed and crushed. The content equivalent to average tablet weight were shaken with methanol (75%) and assayed at 258nm using UV- Visible spectrophotometer (Heliosa UV- Visible spectrophotometer 150, England) [16].

Dissolution Test

The percentage drug release of different formulations of Ketoprofen were carried out using USP <711> dissolution test apparatus (II)[17] (Erweka DT 700, Husenstamm, Germany), using 900ml of phosphate buffer as a medium, at 37^0C $\pm$ 0.5^0C at a speed of 50 rpm. The percentage drug release of Ketoprofen was determined by UV- Visible spectrophotometer (Heliosa UV- Visible spectrophotometer 150, England) at 260nm [16] as shown in table2.

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Comparison of dissolution profiles

Dissolution profiles were compared by means of USP<711> dissolution test apparatus II (Erweka DT 700,Husenstamm, Germany) using immediate release core tablet (Reference) at 50 rpm, using 900 ml of each of the following dissolution media: 0.1N HCL, phosphate buffer pH 4.5 and pH 6.8 at 37 ± 0.5^0C. Approximately 10ml of sample was withdrawn and filtered from each vessel at 10, 15, 20, 30, 45, 60, 90 and 120 min and substituted with 10ml of fresh medium, dissolved Ketoprofen concentrations were determined by UV spectrophotometer (Heliosa UV- Visible spectrophotometer 150, England) at 260 nm.

Analysis of data

Model- Dependent Methods

Data gathered from in vitro dissolution studies were built-in into a variety of kinetic models which were: *first order* (Eq.6) as log cumulative percentage drug remaining *vs.* time, Higuchi *model* (Eq.7) as cumulative percentage drug release *vs.* square root of time, *Hixson – Crowell cube root law* (Eq.8) as cube root percentage drug remaining *v*s. time and *Weibull model* (Eq. 9) as log dissolved amount of drug *v*s. log of time as indicated in table 3, 4 and 5.

First – Order kinetics [18]

$$\text{Log } Q = \text{Log} Q_0 - \frac{kt}{2.303} \qquad (6)$$

Where Q_o is the original concentration of drug, *k* is the first order rate constant and *t* is the time.

Higuchi model.

$$Q = kt^{\frac{1}{2}} \qquad (7)$$

Where *k* is the Higuchi release rate constant and *t* is the time (hr).

Hixson – Crowell cube root law.[19]

$$Q_0^{1/3} - Q_t^{1/3} = K_{HC} \times t \qquad (8)$$

Where Q_0 is the early concentration of drug in the tablet, Q_t is the concentration of drug release at time *t* and K_{HC} is the Hixson – Crowellrate constant.

Weibull model.

An equation described by Weibull was used to explain release procedure [20]. This equation can be used to all types of drug release curves [21,22]. The accumulated fraction of drug release, *m*, in solution at time, *t*, is presented as:

$$m = 1 - \exp\left[-\frac{(t-Ti)^{\beta}}{\alpha}\right] \qquad (9)$$

In the above equation, α, is thetime process, T_i is the lag time, in various cases zero and β is the parameter of shape, (b=1) illustrates the curve as exponential, (b>1) demonstrates S-shaped with upward curve followed by turning point, or (b<1) parabolic with the higher initial slope and after that consistent with the exponential.

Eq.9 is arranged as:

$$\text{Log}[-\ln(1-m)] = b \log(t - Ti) - \log\alpha \qquad (10)$$

Drug release will be linear when log dissolved amount of drug plot *v*s. log of time [18].

Model-Independent Method

Similarity Factor (f_2)

Model – independent method can be classified into pair-wise procedures like similarity factors and ratio testslike mean dissolution time [18]. f_1 (difference factor) and $f_2$similarity were described by different scientists [23]. These equations are approved by the FDA for dissolution profile comparison. Mainly, the similarity factor (f_2) equation is the most widely used method to compare the dissolution method data [24]. This can be expressed as:

$$f_2 = 50 \times log\left\{\left[1 + \left(\frac{1}{N}\right)\sum(Ri - Ti)^2\right]^{-0.5}\right\} \times 100 \qquad (11)$$

Where *N* is the number of samples, $R_i$and *Ti* are the percentage drug release of the reference and test formulations at each time interval. Dissolution profiles of test and reference formulations would be similar when f_2 is greater than 50as shown in table 6 and 7.

RESULTS AND DISCUSSION:

Assessment of Powder Blends and Tablets

Authors reported the influence of flow properties of powders during the manufacturing of tablets [25]. In the present study the flow properties were assessed by different parameters. The angle of repose, Hausner's ratio and Carr's Index of all the formulations were ranged from 28.44± 0.26^0 to 30.54^0± 0.42, 1.17± 0.00 to 1.19± 0.00 and 14.68± 0.35 to 16.43±0.06% respectively. Results indicated that powder blends having low values of angle of repose and Carr's index showed better flow properties and good compressibility. Powders with such properties were capable to produce tablets with low weight variation.

The manufacturing of a water dispersible tablet is difficult. Since these tablets should rapidly disintegrate upon placement in the water [5]. Various physical properties of tablets such as hardness, friability and tablet porosity are strongly linked with rapid disintegration of tablets [26]. In the present work all the blends of fast dispersible formulations were compressed individually by direct compression method. The shape and size of tablets influenced the disintegration and % drug release of tablets. The shape of tablet was round. The colour of tablet was white. Aspartame was added as a sweetener in all the formulations to yield palatable feel. The mean thickness, diameter and hardness of formulations were found to be in the range from 2.15 ± 0.02 to 2.59 ± 0.09 mm and 8.44 ± 0.04 to 8.49 ± 0.02 mm and 3.31 ± 0.17to 4.39 ± 0.11 kg respectively. Results of weight variation indicated that due to the uniform filling of die cavity, the percentage deviation of weight variation were in the acceptable limits.

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The mean tablet weights were ranged from 121.21 ± 1.66 to 206.10 ± 1.07 mg. Similarly, the % friability of all the formulations complies, as none of the formulation exceeded 1% loss in the weight of tablets. The % friability was ranged from 0.31-0.61%. In the present study the average percent assay were ranged from 99.69 ± 0.53 to 101.26 ± 0.38 %. Similarly, all the formulations pass the test for finess of dispersion as expressed in table 2.

Disintegration and Dissolution Studies

Tablets which disintegrates rapidly usually exhibits a number of excipients which are involved in a series of drug release processes which starts when the solvent interacts with the solid and diffuse in the tablet matrix [27]. Super disintegrant are added in the formulations in order to enhance the phenomenon of disintegration [28]. Ac-di-sol facilitate it's disintegration mechanism by swelling and wicking [29]. The swelling capability of Ac-Di-Sol was depended on the ionic strength and the pH of the medium. The swelling was lower at elevated ionic strength and in acidic environment of the medium but was considerably high than the swelling of the other compounds [30]. Tablet porosity strongly affects the disintegration time of water dispersible formulations[5].Rate of water uptake and swelling of superdisintegrants could be affected by numerous physicochemical characteristics of the particles [31]. In the present study all the formulations disintegrated in less than 3 min. The disintegration time were ranged from 19sec-120sec. Results of Physico-chemical tests of all the formulations indicated that disintegration and drug release processes were strongly affected by the amount of binders and disintegrants used. High percentage of Ac-di-sol decreases the disintegration time of formulation F-1, F-2, F-6, F-8 and F-9. Similarly, elevated quantities of Ludipress increases the disintegration time of formulation F-4 and F-5. F-3 and F-7 having low levels of disintegrant showed increase disintegration time. Rapid penetration of liquid dose not always predicts excellent dissolution features and may not be in accordance with disintegration time since the drug release may be affected by numerous other factors too [12]. Percentage drug release was observed in the range from 99.26 ± 0.94 to 102.31± 0.77 % for F1-F9. Results of all the nine formulations were found to be in the acceptable limits. F-6 was particularly selected on the basis of it's pharmaceutically important parameters. F-6 having tablet weight of 122.34 ± 1.08 mg showing the significant drug release which was 99.26 ± 0.94 % after 45min, 99.86 ± 0.50 % drug content also it showed the least disintegration time of 19sec as shown in table 2.

In the present study Ketoprofen is selected as a model drug, having a pK_a of 4.6. Scientists have reported that Ketoprofen showed low solubility and dissolution at acidic environment but as soon as the compound is emptied in to the basic region (upper small intestine), presence of bile salts and rise in pH, improves both the solubility and dissolution dramatically [32]. In the present research, dissolution profiles were also compared in three different dissolution media i.e. 0.1N HCL, phosphate buffer pH 4.5 and pH 6.8. Results indicated that the % drug release of all the formulations in pH 1.2 and 4.5 were less than 85% after 120 min but in phosphate buffer pH 6.8, F5 showed 82% drug release after 30 min as expressed in Figure 1, 2 and 3.

Drug release kinetics

Model-Dependent Method

For the illustration of dissolution data different mathematical models have been used as shown in table 3, 4, 5, 6 and 7 which elucidates the release kinetics of all the formulations in different dissolution media. First-order kinetic model (Eq.6) can be used for the evaluation of dissolution data [33]. This model has been used to explain absorption and / or elimination of various compounds [34]. The value for first-order (Eq. 6) having determinant coefficient (r^2) in 0.1N HCL for F-6 having (r^2 = 0.978) and for phosphate buffer pH 4.5, F-5showed (r^2 =0.993).

Higuchi [19,35] developed numerous models to describe the discharge of water soluble and low soluble compounds integrated in solid and /or semisolid matrixes [18]. In the present study, for Higuchi model (Eq.7) in 0.1N HCL, F-6 having (r^2 =0.992) and for pH 4.5, F-5 having (r^2 = 0.991) was best fitted to the model. For Hixson-Crowell model (Eq. 8), the determinant coefficient (r^2) values in 0.1N HCL and pH 4.5 were ranged from 0.831 to 0.969 and 0.796 to 0.990 respectively. When Hixson-Crowell model is used, it is supposed that the rate of release is restricted by the release of the particle and not dependent upon the diffusion [18]. In tablets, the interaction between drug release and disintegration is multifaceted and it needs model which are appropriate for dissolution profiles of S-shaped. Weibull model illustrate S-shaped drug release profiles [20]. This model explains the category of drug release and time of dissolution [36]. For Weibull model (Eq. 9), the parameter β was < 1 for all the formulations in three different dissolution media, indicating a parabolic curve with steeper initial slope that was constant with the exponential. In the present work, Weibull model is fitted to F1-F9 in 0.1N HCl and in pH 4.5 and F-3 having (r^2= 0.980) and F-5 (r^2=0.976) in pH 6.8.

Model - independent method

Dissolution profiles were compared with the best formulation i.e. F-6 using the similarity factor (f_2). The profiles of all the formulations were similar with the reference profile (F-6) in all the three media. Similarly, dissolution profiles of all the formulations were also compared with immediate release (reference) product using the similarity factor (f_2) in above media. Results showed that the profile of reference formulation was similar with F1-F9 in 0.1N HCL and phosphate buffer pH 4.5 as expressed in table 4 and 5.

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Table 1:Composition of Ketoprofen 100mg tablets

INGREDIENTS (mg/ tablet)	FORMULATIONS								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ketoprofen	100	100	100	100	100	100	100	100	100
Aspartame	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Ludipress	55	20	20	90	90	15	55	55	100
Ac-di-sol	2.75	6.5	0.5	5	0.5	5	0.25	7	5
Quantity per Tablet (mg)	159.4	128.2	122.2	196.7	192.2	121.7	156.8	163.7	206.7

Table 2: Physical Assessments of Formulations

	F1	F2	F3	F4	F5	F6	F7	F8	F9
Repose Angle (n=3)	30.54±0.42	30.49±0.33	29.34±0.23	8.47±0.24	30.44±0.15	29.31±0.22	28.44±0.26	28.71±0.19	28.55±0.17
Carr's Index (%) (n=3)	16.04±0.04	16.43±0.06	14.77±0.18	16.42±0.34	15.37±0.16	14.68± 0.35	15.70± 0.21	16.50± 0.32	16.42± 0.21
Hausner's Ratio (n=3)	1.18± 0.00	1.18± 0.01	1.17± 0.01	1.18± 0.00	1.19± 0.01	1.17± 0.00	1.17± 0.00	1.18± 0.01	1.19± 0.00
Thickness (mm)(n=20)	2.34 ±0.12	2.15 ±0.02	2.15 ±0.06	2.59 ±0.09	2.55 ± 0.12	2.16 ± 0.02	2.30 ± 0.13	2.47 ± 0.154	2.48 ±0.236
Diameter (mm)(n=20)	8.49 ± 0.02	8.48 ± 0.02	8.45 ± 0.04	8.44 ± 0.04	8.46 ±0.03	8.45 ± 0.04	8.45 ±0.04	8.47 ± 0.03	8.45±0.04
Weight (mg)(n=20)	159.74 ± 1.38	129.01 ± 1.93	121.21 ± 1.66	197.01 ±0.78	192.25 ± 1.02	122.34± 1.08	156.92 ±1.07	163.67 ± 0.85	206.10 ±1.07
Hardness (kg) (n=20)	4.33 ± 0.03	3.31 ± 0.17	3.59 ± 0.05	3.48 ± 0.22	3.51 ± 0.13	4.39 ± 0.11	3.42 ± 0.14	3.42 ± 0.18	4.412 ± 0.12
Friability (%) (n=10)	0.52	0.37	0.61	0.31	0.45	0.58	0.49	0.36	0.38
Disintegration (sec) (n=6)	34.8 ± 0.75	30 ± 0.89	77.3 ± 0.81	64.5 ± 1.04	90.8 ±0.75	19.16± 0.75	120.66 ±0.81	23.33 ± 0.81	43.83 ± 0.75
Assay (%) (n=20)	99.69 ±0.53	99.71 ± 1.50	99.79 ± 0.46	100.44 ±0.71	101.24 ± 0.74	99.86 ± 0.50	101.26 ±0.38	100.46 ± 0.83	100.64 ±0.80
Drug Release (%) (n=6)	102.31± 0.77	101.74 ±0.71	101.47 ±0.94	100.13 ±0.91	100.39 ±0.91	99.26 ± 0.94	100.30 ±0.83	100.69 ± 0.88	100.45 ±1.62
Dispersion Test	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes

Table 3:Release Kinetics of nine formulations (F1-F9) in pH 1.2

FORMULATIONS	FIRST ORDER		HIGUCHI		HIXON CROWELL		WEIBULL MODEL		
	r^2	$k_1(h^{-1})$	r^2	$k_H(h^{-1/2})$	r^2	$k_{HC}(h^{-1/3})$	r^2	β	α
F1	0.943	0.013	0.915	7.413	0.912	0.003	0.985	0.613	11.575
F2	0.957	0.012	0.935	7.178	0.931	0.003	0.989	0.598	11.630
F3	0.959	0.007	0.980	5.587	0.944	0.002	0.988	0.663	26.668
F4	0.934	0.010	0.925	6.694	0.910	0.002	0.987	0.549	10.459
F5	0.958	0.006	0.989	5.069	0.944	0.002	0.981	0.767	50.705
F6	0.978	0.005	0.992	4.737	0.969	0.002	0.994	0.687	37.775
F7	0.880	0.005	0.941	4.606	0.863	0.001	0.945	0.628	30.706
F8	0.852	0.006	0.901	5.129	0.831	0.002	0.936	0.576	20.239
F9	0.954	0.007	0.971	5.651	0.939	0.002	0.988	0.616	20.682

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Table 4:Release Kinetics of nine formulations (F1-F9) in pH 4.5

FORMULATIONS	FIRST ORDER		HIGUCHI		HIXON CROWELL		WEIBULL MODEL		
	r^2	$k_1(h^{-1})$	r^2	$k_H(h^{-1/2})$	r^2	$k_{HC}(h^{-1/3})$	r^2	β	α
F1	0.835	0.010	0.796	6.593	0.796	0.002	0.943	0.477	6.740
F2	0.927	0.008	0.916	6.149	0.905	0.002	0.991	0.448	6.880
F3	0.914	0.008	0.906	6.108	0.891	0.002	0.985	0.464	7.715
F4	0.818	0.010	0.767	6.416	0.780	0.002	0.939	0.419	4.702
F5	0.993	0.005	0.991	4.570	0.990	0.002	0.994	0.744	51.377
F6	0.972	0.010	0.982	6.737	0.954	0.003	0.992	0.735	27.538
F7	0.890	0.006	0.928	5.353	0.870	0.002	0.958	0.590	20.127
F8	0.875	0.009	0.847	6.186	0.844	0.002	0.971	0.426	5.748
F9	0.918	0.010	0.891	6.712	0.891	0.002	0.982	0.484	6.866

Table 5:Release Kinetics of nine formulations (F1-F9) in pH 6.8

FORMULATIONS	FIRST ORDER		HIGUCHI		HIXON CROWELL		WEIBULL MODEL		
	r^2	$k_1(h^{-1})$	r^2	$k_H(h^{-1/2})$	r^2	$k_{HC}(h^{-1/3})$	r^2	β	α
F1	0.698	0.004	0.674	3.470	0.686	0.001	0.852	0.112	1.044
F2	0.667	0.003	0.645	3.327	0.656	0.001	0.865	0.106	1.046
F3	0.907	0.017	0.804	6.815	0.866	0.003	0.980	0.427	3.238
F4	0.876	0.002	0.869	2.782	0.873	0.000	0.947	0.069	0.958
F5	0.896	0.022	0.736	6.221	0.844	0.004	0.976	0.394	2.223
F6	0.770	0.003	0.757	3.345	0.763	0.001	0.913	0.104	1.152
F7	0.605	0.007	0.548	4.641	0.576	0.001	0.844	0.216	1.593
F8	0.720	0.002	0.704	3.104	0.711	0.001	0.902	0.092	1.106
F9	0.680	0.003	0.649	3.132	0.667	0.001	0.908	0.097	0.867

Table 6:$f_2$values of F6 (Reference) with (F1-F5 and F7-F9) fast dispersible Ketoprofen 100mg Tablets in three different media

FORMULATION	0.1N HCL		pH 4.5 buffer		pH 6.8 buffer	
	f_2	Dissolution Profile	f_2	Dissolution Profile	f_2	Dissolution Profile
F1	51.60	Similar	62.65	Similar	86.17	Similar
F2	53.22	Similar	68.84	Similar	89.35	Similar
F3	79.34	Similar	72.18	Similar	73.39	Similar
F4	55.57	Similar	56.66	Similar	94.16	Similar
F5	94.60	Similar	62.88	Similar	66.71	Similar
F7	92.22	Similar	75.76	Similar	86.71	Similar
F8	81.89	Similar	63.68	Similar	99.54	Similar
F9	74.62	Similar	63	Similar	74.15	Similar

Table 7:$f_2$values of all the nine formulations (F1-F9) with immediate release core tablet (Reference) Ketoprofen 100mg Tablets in three different media

FORMULATION	0.1N HCL		pH 4.5 buffer		pH 6.8 buffer	
	f_2	Dissolution Profile	f_2	Dissolution Profile	f_2	Dissolution Profile
F1	51.59	Similar	59.86	Similar	44.93	Dissimilar
F2	53.06	Similar	64.52	Similar	45.36	Dissimilar
F3	76.39	Similar	67.28	Similar	47.33	Dissimilar
F4	55.12	Similar	54.21	Similar	45.94	Dissimilar
F5	87.49	Similar	64.11	Similar	42.41	Dissimilar
F6	81.83	Similar	92.47	Similar	47.45	Dissimilar
F7	79.93	Similar	77.37	Similar	46.76	Dissimilar
F8	76.10	Similar	60.27	Similar	47.37	Dissimilar
F9	71.86	Similar	59.76	Similar	42.52	Dissimilar

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Figure 1: Dissolution profiles of nine formulations in 0.1N HCL.

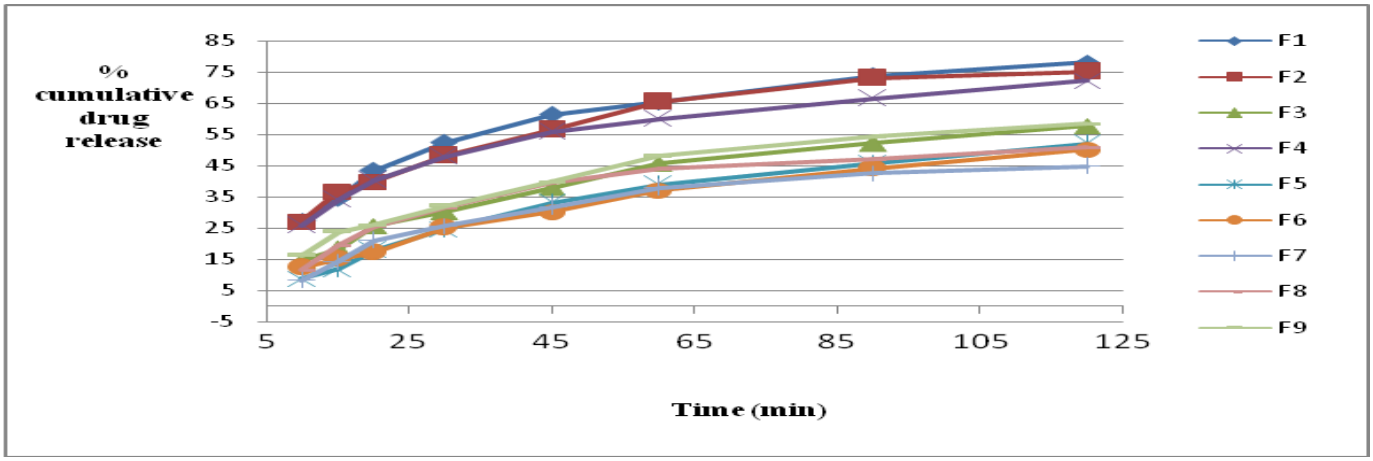


Figure 2: Dissolution profiles of nine formulations in pH 4.5 buffer

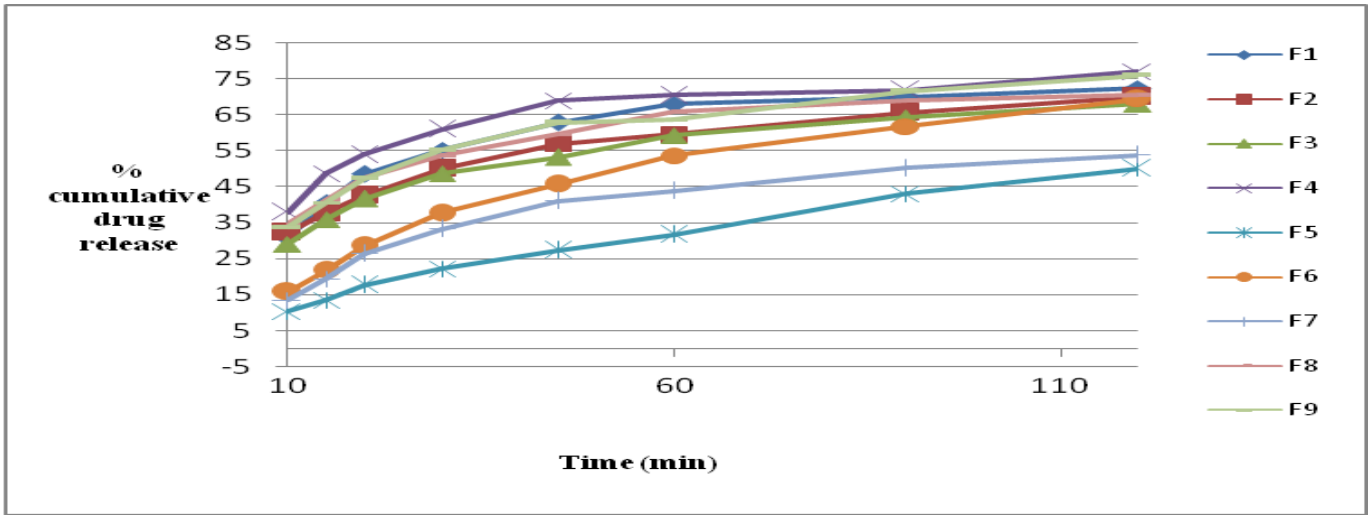
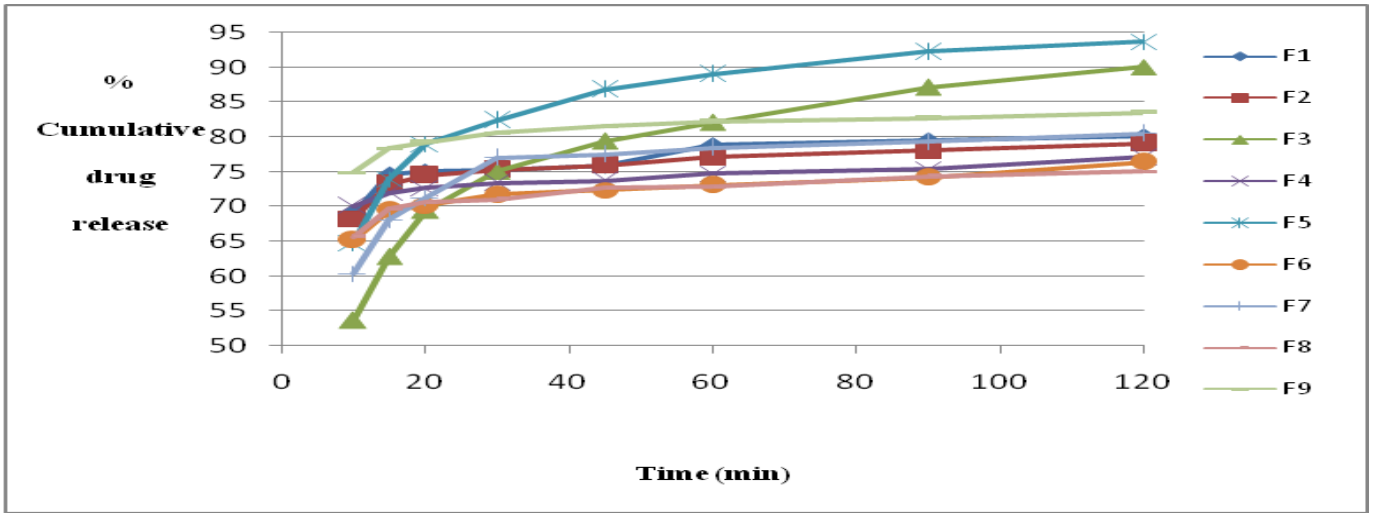


Figure 3: Dissolution profiles of nine formulations in pH 6.8 buffer.



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CONCLUSION

The developed fast dispersible tablet formulations have suitable properties that differentiate them from conventional solid dosage form. Presence of super disintegrants in formulation blends facilitates fast dispersion of tablets. From the present investigation it was found that fast dispersible Ketoprofen tablets can be manufactured by direct compression method and will add to improve tablet administration to patients having chewing and swallowing complications.

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