

FLURBIPROFEN FAST DISINTEGRATING TABLETS

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Received: 05 Dec 2013, Revised and Accepted: 05 Feb 2014

ABSTRACT

Objective: The aim of the present study is to formulate Flurbiprofen Fast Disintegrating Tablets (FFDTs) to improve the dissolution rate and bioavailability. Fast Disintegrating Tablets (FDTs) are solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly within few seconds when placed up on tongue. 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. Flurbiprofen is a non-steroidal anti-inflammatory drug (NSAID), with analgesic, antipyretic and anti-inflammatory effects, mainly by inhibiting prostaglandin synthetase.

Methods: Since, Flurbiprofen is poorly water soluble drug, different formulation techniques were tried for formulation of FDTs, molecular dispersion granulation technique was employed to optimize the formulation by using gelatin as a dispersing agent and sodium lauryl sulfate (SLS) as solubilizing agent. FFDTs were prepared by employing superdisintegrants like Croscarmellose sodium (CCS), Sodium starch glycolate (SSG) and Crospovidone (CP) at different concentrations (3, 5 & 7%). The prepared tablets were evaluated for their physical characteristics and in-vitro dissolution studies. The best formula was subjected to the anti-inflammatory activity studies in rats using paw-edema method.

Results: The results showed that; all formulations of FFDTs had weight variation and drug content within the pharmacopoeial limits, hardness of 4.21 ± 0.0270 to 4.90 ± 0.0581 kg/cm², friability was less than 1%, in vitro disintegration time of 12.75 to 72.34 seconds, wetting time of 10.50 to 46.00 seconds, and in-vitro drug release showed maximum release of 100.32% after 6 minutes for tablets contain 7% CP. While, the highly retarded release of 58.15% at the end of 10 minutes with 3% CCS. The standard formulation without superdisintegrant (F10) showed 48.80% drug release at the end of 10 minutes.

Conclusion: Among all formulations, promising formulation (F9) which contains 7% CP, appeared to be the best formula as it showed good wetting time (10.50 sec.), fastest disintegration time (12.75 sec.), maximum drug release of 100.32% within 6 minutes and superior anti-inflammatory activity.

Keywords: Flurbiprofen; Fast disintegrating tablets; Superdisintegrants; Anti-inflammatory effect.

INTRODUCTION

Tablets are the most widely used dosage form because of its convenience in terms of self-administration, compactness and easy in manufacturing [1]. Fast disintegrating tablets are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in oral cavity within a minute without the need of water or chewing. These are not only useful in administration of drugs in pediatric and geriatric patients but in patients suffering from dysphagia, leading to improved patient compliance [2]. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people [3].

Orally disintegrating tablets have been found to be the choice for Psychiatric as well as patient suffering from stroke, thyroid disorder, Parkinson's diseases and multiple sclerosis, patients with nausea, vomiting and motion sickness [4]. The advantages of fast dissolving tablets include easy manufacturing, accurate dosing and easy handling by patients, no requirement of chewing and water for swallowing [5]. These dosage forms have been investigated for their potential in improving bioavailability of poorly soluble drugs through enhancing the dissolution profile of the drug and also for hepatic metabolism drugs [6]. For these formulations, the small volume of saliva is usually sufficient to result in tablets disintegration in oral cavity. The medication can then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from gastrointestinal tract.

The excipients employed in fast dissolving tablets are always hydrophilic in nature whereas drug may be either hydrophilic or hydrophobic. If the drug is hydrophilic, the dosage form is known as fast dissolving tablets otherwise if drug is hydrophobic it is known as fast disintegrating tablets [7]. The various synonyms used for fast dissolving tablets include mouth dissolving tablets, orally disintegrating tablets, melt in-mouth tablets, porous tablets, oro-

dispersible, quick dissolving and rapid disintegrating tablets [8]. The various techniques used for manufacturing of rapidly disintegrating or dissolving tablets are Freeze drying, Spray drying, Molding, Mass extrusion, Melt granulation, Sublimation and Direct compression [9]. Direct compression is one of these techniques which require incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration [10 & 11]

The basic approach in development of fast dissolving tablets is the use of superdisintegrants like Cross linked carboxymethylcellulose (Croscarmellose), Sodium starch glycolate (Primogel, Explotab). Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. Superdisintegrants provide fast disintegration due to collective effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution [12-14]. The objective of the present study is to enhance the dissolution rate of Flurbiprofen tablets using superdisintegrants. Flurbiprofen is selected as the model drug which comes under Non steroidal anti-inflammatory drug (NSAIDs) class. Flurbiprofen is a member of the phenylalkanoic acid derivative family of NSAIDs, which are widely used for the long-term treatment of chronic rheumatic diseases such as rheumatoid arthritis, osteoarthritis and ankylosing spondylitis [15]. It is effective in inhibiting surgically induced miosis in human eyes while cataract extraction [16 & 17].

It has also caused a dose dependent inhibition of collagen-induced platelet aggregation in patients with platelet-rich plasma [18]. Flurbiprofen is approximately 99% plasma protein bound and has an elimination half life of 3 to 6 hours. It undergoes hydroxylation and conjugation in the liver and is mainly excreted in the urine [19]. It is classified as poorly water soluble class II drug and it is primarily intended to treat painful conditions, which requires fast release of drug [20].

Since, molecular dispersion granulation technique was employed by using gelatin as a dispersing agent and sodium lauryl sulfate as solubilizing agent to improve its release. This technique was made to develop the Flurbiprofen rapidly disintegrating tablets which disintegrate in the oral cavity without the need of water within seconds.

This will lead to the formation of suspension / solution form which can be easily swallowed, thereby improving dissolution rate and bioavailability of drug and onset of pharmacological actions.

MATERIALS AND METHODS

Materials

Flurbiprofen was a gift sample from El-Kahira Pharmaceutical Chemical Company, Cairo, Egypt. All the superdisintegrants and Microcrystalline cellulose (Avicel PH 101), were kindly supplied by Chemical Industries Development Co. (CID), Cairo, Egypt.

Gelatin, Sodium lauryl sulfate, Magnesium stearate, Saccharine sodium and colloidal silicon dioxide (Aerosil), from El-Gomhoria Chemicals Co., Cairo, Egypt, Mannitol and Carrageenan (Type I), from Sigma Aldrich, Germany.

All the other chemicals used were of high analytical grade.

Methods

Preparation of Fast Disintegrating Tablets

Fast disintegrating tablets of Flurbiprofen were prepared by the molecular dispersion granulation technique [21], using different

excipients. The excipients used were avicel PH 101 (binding agent), mannitol (diluent), saccharine sodium (sweetening agent), CCS, SSG and CP (superdisintegrants).

The materials like Flurbiprofen, avicel PH 101, mannitol, SLS, CCS, SSG and CP were sifted through # 40 mesh and Aerosil, magnesium stearate was sifted through # 60 mesh and collected separately. According to formula, gelatin and SLS were taken in dish and melted at 70°C, and then drug was transferred into dish under continuous stirring. Once it formed homogenous mixture, it was stored in refrigerator for five hours. Then the cooled mass was milled and mixed with previously sifted avicel PH 101, CCS, CP and/or SSG and mixed for 10 minutes in a mortar and finally, sifted Aerosil and magnesium stearate were added to the mixture and lubricated for 5 minutes. The lubricated mixture was compressed into tablets by using a single-punch tablet compression machine (Type AR 402, Erweka apparatus, Heusenstamm, Germany) equipped with a flat faced 8 mm punches. The machine was adjusted to produce tablets of 200 mg in weight and each contains 50 mg of Flurbiprofen. The standard Flurbiprofen tablets (F10) were prepared in a similar manner without using superdisintegrants.

Mannitol was employed as a diluent as it has negative heat of solution which imparts a unique cooling sensation and pleasant taste when used in formulations for tablets intended to dissolve in the oral cavity [22]. The reasons for selection of CP are its high capillary activity, pronounced hydration capacity and little tendency to form gels [23]. SSG was chosen because of its higher swelling capacity [24]. CCS was used as it has fibrous particles that acts as channels to absorb water allowing rapid disintegration [25]. The composition of each of the prepared tablet formulations is shown in Table 1

Table 1: It shows the formulation composition of Flurbiprofen fast disintegrating tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Flurbiprofen	50	50	50	50	50	50	50	50	50	50
Gelatin	2	2	2	2	2	2	2	2	2	2
SLS	2	2	2	2	2	2	2	2	2	2
Mannitol	114	110	106	114	110	106	114	110	106	120
Avicel PH 101	20	20	20	20	20	20	20	20	20	20
CCS	6	10	14	-	-	-	-	-	-	-
SSG	-	-	-	6	10	14	-	-	-	-
CP	-	-	-	-	-	-	6	10	14	-
Saccharine Sodium	2	2	2	2	2	2	2	2	2	2
Aerosil	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200	200	200	200	200

Evaluation of Physical Parameters

All batches of tablets were evaluated for various parameters like weight variation, friability, hardness, drug content, disintegration, wetting Time, water absorption ratio and dissolution.

Weight variation test

For determining weight variation, 20 tablets of each formulation were weighed using an electronic weighing balance (An electric balance, Mettler, AJ 100, (Switzerland) [26].

Friability test

Six tablets from each batch were examined for friability using Roche friabilator (Tablet friability test apparatus, (model; FT-2D) VEEGO, Progressive Instruments, Bombay, India). The pre-weighed tablets were rotated at 25 rpm for 4 min or total 100 revolutions, the tablets were then reweighed and the percentage of weight loss was calculated by the following equation: % Friability = Initial weight – Final weight / Initial weight X 100 [27].

Hardness test

The hardness of the tablet was determined using Erweka hardness tester. A tablet is placed in the hardness tester and load required to crush the tablet is measured. Three tablets from each formulation

batch were tested randomly and the average reading was calculated [28]. Hardness is expressed in kg/cm².

Drug Content Determination

For assessment of drug content, ten tablets were powdered, and the aliquot of powder equivalent to 50 mg of drug was dissolved in appropriate quantity of methanol and 1.2 pH buffer solution [29]. The solution was then filtered, properly diluted and the absorbance was measured spectrophotometrically at 247 nm (Jenway LTD, UK, Felsted, Dunmow, Essex, CM63LB, (Model: 6105 UV/ Vis), England) and then Flurbiprofen content of each tablet was calculated

In vitro Disintegration Time

The test was carried out on six tablets using distilled water at 37°C ± 2°C as disintegration medium and the time taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus (Tablet disintegration test apparatus,(VEEGO), Model: VTD-3D, India) was measured in seconds [30].

Wetting Time and Water Absorption Ratio

The wetting time of the prepared tablets was measured using a simple procedure. In this method, a filter paper of 10 cm diameter was placed in a petri dish, with diameter of 10 cm, followed by addition of ten milliliters of water containing methylene blue. A

tablet from each formulation was carefully placed on the surface of the filter paper.

The time required for water to reach the upper surface of the tablets was recorded using stop watch and taken as the wetting time. To check for reproducibility, these measurements were carried out in triplicates and the mean values were calculated [31] and the water absorption ratio (W.A.R) was calculated using the following Equation: $W.A.R = 100 (W_a - W_b) / W_b$ [32]. Where, W_b and W_a are the weight before and after water absorption respectively.

In vitro Dissolution Study

The in vitro dissolution studies of Flurbiprofen tablets was carried out using USP type II (paddle) apparatus (Dissolution SRS-Plus, Hanson Virtual Instrument, U.S.A) at a rotation speed of 50 rpm. The drug release studies were carried out using 900 ml of 0.1 N HCl, pH 1.2 buffer as dissolution medium at $37 \pm 0.5^\circ\text{C}$ [33]. An aliquot of 5 ml was withdrawn at predetermined time intervals of 1, 2, 4, 6, 8, 10 minutes and replaced with fresh dissolution medium.

The samples were filtered, by passing through $0.45 \mu\text{m}$ membrane filters, suitably diluted and analyzed at 247 nm [34] using UV-Visible spectrophotometer [Jenway LTD, UK, Felsted, Dunmow, Essex, CM63LB, (Model:6105 UV/ Vis), England], then concentration of the drug was determined from standard calibration curve.

Kinetics and Mechanism of Drug Release

To understand the mechanism of drug release of different formulae of flurbiprofen tablets, the data were treated according to zero-order (cumulative amount of drug released vs time), first-order (log cumulative percentage of drug released vs. time), and Higuchi's (cumulative percentage of drug released vs. square root of time) equations [35& 36].

Anti-inflammatory activity of Flurbiprofen Fast Disintegrating Tablets

Animals

Adult male albino rats, weighing ($200 \pm 20 \text{ gm}$), were used in this study, and the study was approved by the Institutional Animal Care and Use Committee. The rats were housed in groups and kept fastened for 24 hours prior to the experiments but were allowed free access to water. The rats were divided into 3 groups each group composed of 6 animals. First group (Standard group) was administered (F10) orally.

The second group (Test group) was administered Fast disintegrating tablets of Flurbiprofen (F9) according to the dose of 3.8 mg/kg [37]. while the (controlled group) animals were given saline (0.9% NaCl) containing no drug. After 30 minutes of oral administration of formulations and plain Flurbiprofen, 0.1 ml of 1% w/v carrageenan (in 0.9% normal saline) was injected in the sub planter region of the right hind paw of rats.

Carrageenan induced Paw Edema Method

Anti-inflammatory activity was measured using carrageenan induced rat paw oedema assay [38].

Tablets containing 7% CP (F9) have the shortest disintegration time and the highest in-vitro release (F9) was chosen for anti-inflammatory study. The thickness of the injected paw was measured immediately after carrageenan injection and after 0.5, 1, 2 and 3 hours using a micrometer (Dial Micrometer Model 120-1206 Baty and Co. Ltd., Sussex, (England).

The % inhibition of edema induced by carrageenan was calculated for each group using the following equation: % inhibition in edema thickness = $\{1 - (T_t/T_c)\} \times 100$ [39& 40].

Where: T_t = mean increase in thickness of carrageenan paw edema of treated groups, T_c = mean increase in thickness of carrageenan paw edema of control groups.

Anti-inflammatory activity was measured as the percentage reduction in oedema level when drug was present, relative to control [41].

Statistical analysis

The experimental data are statistically analyzed using one-way analysis of variance (ANOVA) followed by Tukey (post tests) to determine if the differences between the results of the investigated samples are significant or not. Difference was considered significant when $*P < 0.05$.

RESULTS AND DISCUSSION

Evaluation of Physical Parameters of Flurbiprofen Fast Disintegrating Tablets (FFDTs)

The characteristics of prepared FFDTs are shown in Tables (2& 3) and Figures (1& 2).

Weight variation

The average weight was found in all designed formulations in the range 196.4 ± 0.7694 to $206.2 \pm 0.9381 \text{ mg}$. All the tablets passed weight variation test as the tablet weight was more than 130 mg and less than 324 mg , hence 7.5% maximum difference allowed i.e. in the pharmacopoeia limits [42].

Friability test

The friability of all formulations was found to be less than 1 % and was in the range of 0.2702 ± 0.0014 to $0.5578 \pm 0.0019\%$ indicating a good mechanical resistance of tablets.

Hardness

The hardness of the prepared tablets was maintained within the range of $4.21 \pm 0.0270 \text{ kg/cm}^2$ to $4.90 \pm 0.0581 \text{ kg/cm}^2$; it was considered adequate for mechanical stability.

Drug Content

The drug content uniformity was performed for all the 10 formulations. The percentage drug content of the tablets was ranged from 98.44 ± 0.63 to $101.90 \pm 0.85\%$ of Flurbiprofen.

Table 2: It shows the physical properties of Flurbiprofen fast disintegrating tablets

Formulae	Physical characteristics			
	Weight (mg)	Friability (%)	Hardness (kg/cm ²)	Drug content (%)
F1	198.8±0.4160	0.3842±0.0034	4.25±0.0274	99.23±0.75
F2	201.0±1.2361	0.2858±0.0028	4.90±0.0581	99.60±0.49
F3	202.4±1.7678	0.2786±0.0026	4.38±0.0370	100.14±0.33
F4	200.7±0.8337	0.3830±0.0016	4.74±0.0365	98.44±0.63
F5	206.2±0.9381	0.4367±0.0040	4.21±0.0270	101.37±0.07
F6	197.9±0.5523	0.4256±0.0021	4.64±0.0469	99.22±0.06
F7	196.4±0.7694	0.2702±0.0014	4.78±0.0676	99.36±0.88
F8	199.6±0.6042	0.4256±0.0021	4.49±0.0164	101.48±0.52
F9	200.0±0.3100	0.5498±0.0011	4.60±0.0310	100.14±0.68
F10	203.3±0.1499	0.5578±0.0019	6.72±0.0265	101.90±0.85

In-vitro disintegration time

The in-vitro disintegration time is measured by the time taken to undergo complete disintegration. It was observed that the disintegration time of the tablets decreased as the concentration of superdisintegrants increased as shown in Fig. 1. The FFDTs made with CCS at 3%, 5% and 7% exhibited the disintegration time of 56.33, 22.67 and 14.31 seconds respectively, where SSG exhibited 72.34, 31.00 and 25.66 seconds respectively at same concentrations and CP made formulations exhibited the disintegration time of 30.50, 21.78 and 12.75 seconds respectively at the same concentration. Formulations F3 and F9 showed rapid disintegration compared to other formulations. Comparatively, the disintegration times of tablets were in the order of CP < CCS < SSG. The faster disintegration of tablets with CP may be attributed to its rapid capillary activity and pronounced hydration [43]. The standard formulation without superdisintegrant (F10) showed disintegration time of 376.67 seconds.

Wetting time and Water absorption ratio

Wetting time is closely related to the inner structure of the tablet. The wetting time of FFDTs were found to be in the range of 10.50±0.56 to 46.00±0.47 sec. Promising formulations F3 and F9 showed a wetting time of 11.39±1.12 and 10.50±0.56 sec. respectively, which facilitate the faster dispersion in the mouth. Comparatively, the wetting times of tablets were in the order of CP < CCS < SSG. The standard formulation (F10) showed wetting time of 330.00±0.27 seconds.

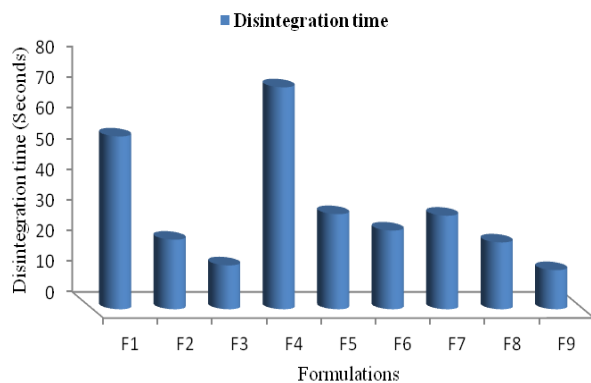


Fig. 1: It shows disintegration time of various formulations of Flurbiprofen fast disintegrating tablets

In-vitro dissolution studies

The dissolution of Flurbiprofen from the tablets is shown in Figures (3-5).

The in vitro drug release profile from formulation batches prepared with CCS was shown in Fig 2. Formulation F1 showed 58.15% drug release after 10 min., F2 and F3 showed 100.35% and 99.98% drug release in 6 min. and 8 min. respectively. It was observed that by increasing the concentration of CCS from 5 to 7%, the rate of drug release decreased

This result was explained by [44], when CCS is added to tablet formulations at a high concentration, its absorption of water might cause an increase in viscosity of the liquid within the tablet, and further water penetration would be delayed, this cause a delay in the dissolution. F2 formulation showed better drug release. The in vitro drug release profile from formulation batches prepared with SSG was shown in Fig 3. Formulations F4 - F6 showed 85.53%, 95.79% and 99.88% drug release after 10 min. From the above observations, it is concluded that by

Water absorption ratio, which is important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water, was calculated. It was found to be in the range of 70.45 to 199.00%.

Table 3: It shows the disintegration time, wetting time and water absorption ratio of Flurbiprofen fast disintegrating tablets

Formulae	Physical characteristics		
	In-vitro disintegration time (sec.)	Wetting time (sec.)	Water absorption ratio (%)
F1	56.33±1.45	41.50±0.23	72.00
F2	22.67±0.54	16.90±1.02	180.52
F3	14.31±1.12	11.39±1.12	198.35
F4	72.34±1.23	46.00±0.47	70.45
F5	31.00±1.26	20.00±0.51	157.87
F6	25.66±1.31	18.31±0.49	172.70
F7	30.50±1.11	23.00±1.01	96.23
F8	21.78±1.38	14.00±0.39	190.59
F9	12.75±1.31	10.50±0.56	199.00
F10	376.67±1.30	330.00±0.27	56.82

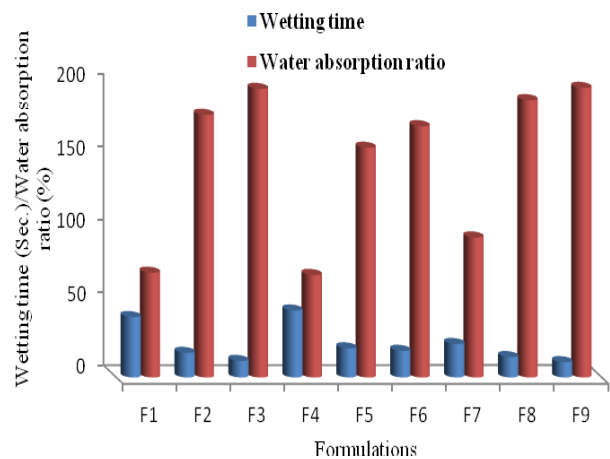


Fig. 2: It shows wetting time and water absorption ratio of various formulations of Flurbiprofen fast disintegrating tablets

increasing the concentration of SSG, the drug releases at faster rate. F6 formulation showed better drug release. The in vitro drug release profile from formulation batches prepared with CP was shown in Fig 4. Formulations F7 showed 100.08% drug release after 8 min., F8 and F9 showed 98.99% and 100.32% drug release in 6 min. respectively. From the above observations, it is concluded that by increasing the concentration of CP, the drug releases at faster rate. F9 formulation showed better drug release. This can be well correlated with the disintegration time and wetting time which were very lower for the formulation with 7% CP (F9) than the other formulations.

The standard formulation (F10) showed 48.80% drug release at the end of 10 minutes. All the formulations showed rapid disintegration and fast dissolution rate when compared with standard formulation. This improvement is due to the presence of superdisintegrant as they provide quick disintegration due to combined effect of swelling and water absorption by tablets [45].

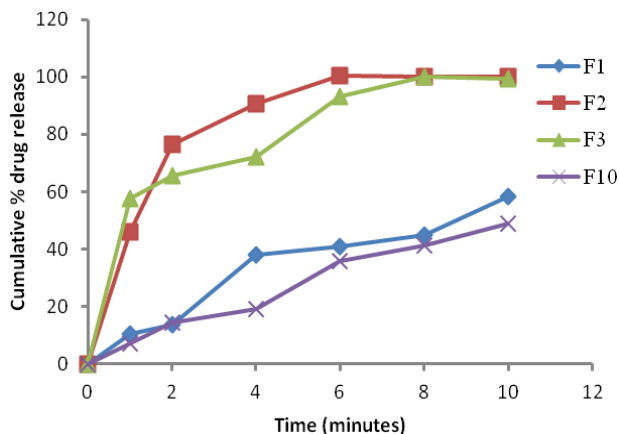


Fig. 3: It shows the dissolution profile of FFDT prepared by using various concentrations of Croscarmellose sodium and standard formula

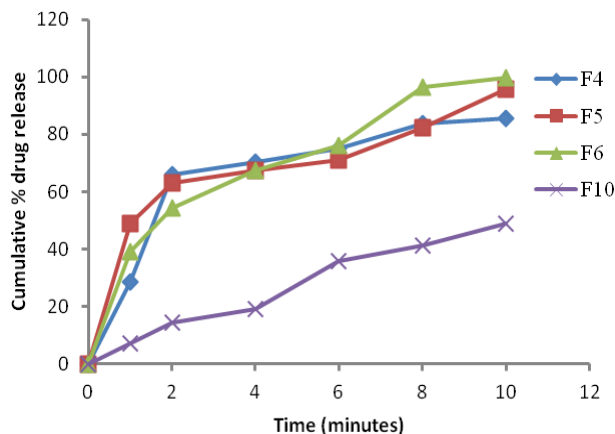


Fig. 4: It shows the dissolution profile of FFDT prepared by using various concentrations of Sodium starch glycolate and standard formula

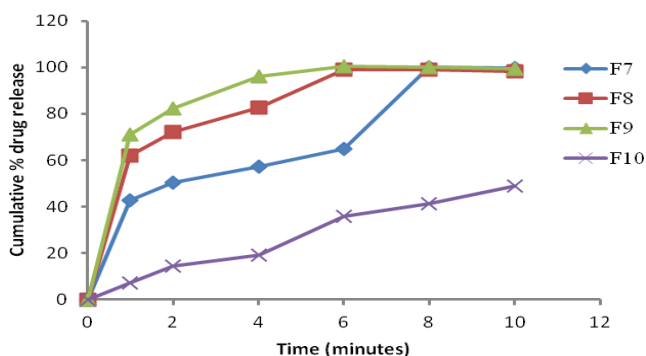


Fig. 5: It shows the dissolution profile of FFDT prepared by using various concentrations of Crospovidone and standard formula

Analysis of release data

Table 4 illustrates the analysis of the release data of Flurbiprofen from the different tablet formulations using zero, first order kinetics and the diffusion model. In our experiments, the in vitro release profiles of drug from formulations (F2,F6,F9 and standard tablets)

could be best expressed by Higuchi's equation, as the plots showed high linearity (R^2), indicating that diffusion is the mechanism of drug release from these formulations. Zero-order drug release was obtained from formulations (F1, F3, F5, F7 and F8). While, First-order drug release was obtained from (F4).

Table 4: It shows the release kinetics of Flurbiprofen from different tablet formulae

Formulation	Order of reaction		
	Correlation coefficient (r^2)		
	Zero	First	Higuchi
1	<u>0.973062</u>	0.95523	0.936098
F2	0.916974	0.91492	<u>0.954204</u>
F3	<u>0.983400</u>	0.86146	0.973837
F4	0.833028	<u>0.93607</u>	0.887580
F5	<u>0.969831</u>	0.89795	0.960747
F6	0.981896	0.89708	<u>0.989863</u>
F7	<u>0.933715</u>	0.78405	0.894604
F8	<u>0.994115</u>	0.91898	0.988857
F9	0.957863	0.93240	<u>0.983828</u>
F10	0.957696	0.97077	<u>0.977706</u>

The underlined value is the highest correlation coefficient which indicates the release mechanism

Anti-inflammatory activity

The anti-inflammatory activity of Flurbiprofen from its selected formula (F9) was studied using the rat hind paw edema technique as the model for inflammation, and compared to the control untreated group.

This formula is selected for testing the anti-inflammatory activity as it shows the fastest disintegration time and highest in-vitro release.

The results of the carrageenan-induced rat paw edema test are shown in Table 5 and Figure 6. Both test and standard groups showed a significant reduction of the carrageenan induced paw edema thickness compared with the control group. It was observed that standard group produced maximum percent edema inhibition after 3 hours (62.38%), while test group produced maximum percent edema inhibition after 2 hours (71.44%). Performing ANOVA test for the tested formulations with regards to the inhibition percentage when compared with the control and

standard, it is found that there was a significant difference between the tested group and control group. Also there was a significant difference between the tested group and standard group at (*P < 0.05) which indicate the superior anti-inflammatory activity of the formulated FFDTs. The development of edema in the paw of the rat after the injection of carrageenan is due to release of histamine,

serotonin and prostaglandin like substances [46]. Significantly high anti-inflammatory activity of FFDTs may be due to inhibition of the mediators of inflammation such as prostaglandin.

The present result indicates the efficacy of FFDTs as an efficient therapeutic agent in acute anti-inflammatory conditions.

Table 5: It shows the percent edema inhibition by administration of different drug formulations

Time (hrs)	% edema inhibition		
	Control group	Standard group	Test group
0.5	0.0	10.81 ^{*a}	31.21 ^{*a,b}
1	0.0	30.59 ^{*a}	45.38 ^{*a,b}
2	0.0	53.27 ^{*a}	71.44 ^{*a,b}
3	0.0	62.38 ^{*a}	60.73 ^{*a}

*P < 0.05: Statistically significant; a: from Control, b: from Standard

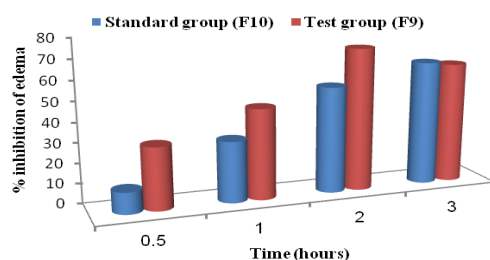


Fig. 6: It shows the comparative % inhibition of edema produced by standard (prepared tablets of Flurbiprofen without super disintegrants) and test (prepared fast disintegrating tablets of Flurbiprofen)

CONCLUSIONS

It can be concluded that fast disintegrating tablets of Flurbiprofen, a non-steroidal anti-inflammatory drug (NSAID) can be successfully prepared by molecular dispersion granulation technique by using different concentrations of selected superdisintegrants; croscarmellose sodium, sodium starch glycolate and crospovidone for the better patients' compliance. The prepared tablets disintegrate within few seconds without need of water; thereby improving dissolution rate and bioavailability of the drug. The results have shown that Crospovidone 7% as a superdisintegrant (F9) showed good wetting time (10.50 sec.), fastest disintegration time (12.75 sec.) and maximum in vitro drug release of 100.32% within 6 minutes, when compared with other formulations. Thus, F9 was considered to be the best formula among the other formulations. Also, there was a significant difference in the anti-inflammatory activity between the prepared tablets (F9) and the standard Flurbiprofen tablet (F10) indicating superior anti-inflammatory activity.

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