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Fast Disintegrating Tablets of Flurbiprofen with Natural Super Disintegrants–Formulation and *In Vitro*, *In Vivo* Evaluation.

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ABSTRACT
Flurbiprofen is a non-steroidal anti-inflammatory drug, non selective COX inhibitor and most effective to hinder the prostaglandin. In this research work, an attempt was made to develop solid dispersions for the enhancement of solubility, dissolution and bioavailability of Flurbiprofen and also to find the effect of natural super disintegrants in the development of fast disintegrating tablets. Solid dispersions were prepared by solvent evaporation method using PEG 6000 as carrier in different ratios. The optimized solid dispersions were utilized in the formulation of FDTs using different natural superdisintegrants in different concentrations. The prepared tablets were evaluated and subjected to in vitro dissolution studies to select the best formulation. All the formulations showed fast disintegrating action. Among all the formulations dehydrated banana powder containing formulations FF5 (96.72) and FF6 (99.27) showed better drug release from the dosage form. Thus, dehydrated banana powder can be utilized as better superdisintegrant in the advancement of quickly breaking down tablets when compared to orange peel pectin and mango peel pectin. Finally the optimized formulations were subjected to pharmacokinetic studies in rabbits. The solid dispersion reached peak concentration (C_{max}) 11445.46ng/ml at T_{max} of 2h while it was observed to be 9140.84ng/ml at t_{max} of 3h in case of control tablet, indicating that enhancement of absorption in solid dispersion pattern of Flurbiprofen than pure form. The AUC of control and FF6 tablets of Flurbiprofen were 31495.16 and 43126.52ng-h/ml correspondingly. These results indicated that the FF6 tablet showed enhancement of AUC when compared to control tablet of Flurbiprofen.
Keywords: *Fast disintegrating tablets (FDTs)*, *Flurbiprofen, PEG 6000, solid dispersion, superdisintegrants.*

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INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. Oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, noninvasive method and ease of administration leading to high level of patient compliance. Fast disintegrating tablet (FDT) is "A strong dose structure contains restorative substances, which break down quickly, for the most part inside an issue seconds, when put up on tongue". FDTs break down as well as disintegrate quickly in spit without the requirement for water [1].

Superdisintegrants are substances which disintegrates the drug within seconds. The major function of disintegrants is to oppose the efficacy of the tablet binder and the physical forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on

i. By capillary action
ii. High swell ability of disintegrants
iii. Capillary action and high swell ability
iv. Chemical reaction (release of gases)

MATERIAL AND METHODS

Flurbiprofen drug was gifted by Aurobindo Pharmaceuticals, Hyderabad, Telangana, India. Mango peel pectin, Orange peel pectin, Banana powder, PEG6000, Avicel PH 102, Aspartame, Mannitol, Talc, Magnesium stearate from local manufacturers.

Construction of standard chart of Flurbiprofen

Adjustment bend of Flurbiprofen was plotted in 6.8 pH phosphate support which was chosen from dissolvability study flurbiprofen was evaluated spectrophotometrically at λ max of 247 nm.

Solubility investigation of Flurbiprofen

As the pH of the spit (medium present in the oral pit) run from 6 to 7.4, the dissolvability of medication was contemplated in solvents of pH 6.8 phosphate supports and refined water. A 100mg of medicine was taken and solubilized in 100 ml of solvents autonomously and the dissolvability was watched. Then an appropriate medium was chosen relying on the dissolvability results.

Compatibility study

Fourier Transform Infrared (FTIR) spectrophotometer was utilized for infrared examination tests to translate association's medication with polymers and different fixings. The spectra of unadulterated medication, bearers and advanced plan were recorded on FTIR (Shimadzu, Japan) utilizing KBr cartridge ranges from 4000cm^{-1} to 400cm^{-1} district. The pellets were incubated with 100 mg potassium bromide with 5mg test pellet at 12,000 psi under vacuum for 3min. The resulting spectra have been eliminated for pinnacles and any potential changes in the spectra.

Differential scanning colorimetry study was completed on flurbiprofen unadulterated medication, bearers and improved definition and thermograms were gotten utilizing DSC (Shimadzu, Japan). Precisely gauged Samples (5-10mg) were set in shut, penetrated, level base aluminum dish. Nitrogen gas was siphoned at stream pace 50 ml/min at steady warming pace of 15ºC/min in scope of 50ºC - 350ºC temperature. The liquefying point, top maxima appearance of any new pinnacles and change fit as a fiddle was noted [1].

Preparation of solid dispersions

The solid dispersion is arranged by utilizing PEG6000 as transporter in the ratios of 1:1, 1:2, 1:3, 1:4 1:5 and 1:6 using acetone as solvent by solvent evaporation method. Drug and bearer were weighed and triturated in mortar and pestle for 5min [4]. This physical mix was then separated in acetone with reliable blending. This dissolvable was dispersed on warming mantle kept up at 45ºC ± 2ºC this model were dried in a desiccators for 24hrs over anhydrous Calcium Chloride. Dried mass was rejected, squashed pummeled and went through sifter 60. Formulae of solid dispersions of flurbiprofen was shown in table 1.

Table 1: Formulae of Solid Dispersions of Flurbiprofen

Solid Dispersion	Flurbiprofen	PEG6000	Ratio
FS1	50	50	1:1
FS2	50	100	1:2
FS3	50	150	1:3
FS4	50	200	1:4
FS5	50	250	1:5
FS6	50	300	1:6

In-vitro drug release study of solid dispersion FS6

In-vitro deterioration examinations promising solid scatterings were performed by USP XXIII Type-II breaking down mechanical get together using at 50rpm paddle stirrer uses 900ml pH 6.8 phosphate support at 37 ± 0.5ºC as breakdown medium. The alcohol content disintegrating medium (5ml) was withdrawn during exposure time (2, 4, 6, 8, 10, 15 & 30 min) was quickly replaced with an equal volume crisp medium. Models were separated by 0.22 film channel plate and investigated for content by estimating absorbance at 247nm. Solution change is fixed from standard change turn and passed on hard fast percent medication isolated. The discharge studies were performed in replicates three [10].

Pre Compression studies: The following pre compression studies were conducted for flurbiprofen and excipient mixture which includes bulk density, tapped density, angle of repose, Hausner ratio, Compressibility index.

Preparation of rapidly disintegrating tablets of Flurbiprofen

Flurbiprofen, basic superdisintegrants like dehydrated banana powder, orange peel pectin, mango powder**,** microcrystalline cellulose, mannitol were correctly measured and experienced 40-work mix for 15 minutes on screen and glass mortar to get uniform sized particles. The get mixture was filled with magnesium stearate powder mixing continued for another 5 minutes. The resulting mixture (See table 2) is compressed into tablets vertically using 12 mm round level up to the punch of the rotary tablet machine.

Evaluation of rapidly disintegrating tablets of Flurbiprofen

The prepared rapidly disintegrating tablets of Flurbiprofen were evaluated for uniformity of weight using 20 tablets [6], hardness (Monsanto tester) using 5 tablets, thickness (vernier calipers) using 5 tablets, friability (Roche friabilator) using 10 tablets [7], drug content using 10 tablets, in vitro dissolution studies using 3 tablets.

Time for in-vitro dispersal

A tablet is set at 10ml pH 6.8 phosphate buffer assay at 37 ± 0.5ºC required for complete dispersion [4].

Consistency of medication content

For the substance consistency test, ten tablets were estimated beat to fine powder, measure powder unclear from 10mg of Flurbiprofen was ousted into refined water fluid was sifted (0.22m film channel plate (Millipore Corporation). The Flurbiprofen substance was coordinated by assessing the absorbance at 247nm (using UV spectrophotometer, Shimadzu 1700) after being reasonably diluted with purified water [11].

Wet time and water absorption ratio (R)

Tissue paper twice broken into petri dish was placed in 5cm diameter with 6ml water. A tablet deliberately placed on tissue paper in petri dish. The time required for water to be completely wet at upper surface of tablet is wetting time [13]. The degree of water intake (R) is chosen by going to the condition:

$R = 100 \times (wa - wb) / wb$

Tablet loads when wb and wa water free at any time.

In vitro drug release study

The in-vitro dissolution study of tablets of flurbiprofen by using USP XXIII Type-II dissolution Contraction (Electrolab, Model TDT-06N) using paddle stirrer at 50 rpm at 37 ± 0.5ºC medium. One tablet was used in each test. Aliquots of separating medium (5 ml) were undoubtedly withdrawn between periods (2, 4, 6, 8, 10, 15 & 30 min) and were quickly separated by an equal volume of new medium. Models were separated by 0.22 film channel plate and checked for content by surveying absorbance at 247nm. [12]

Stability studies of optimized formulation FF6

Considering the excellent concealed stapled glass vases at 40ºC / 75% RH over period of 3 months, tablets representing FF6 have been introduced with activated consistency. Over a period of several months, the tablets were clearly checked for any physiological changes that were observed for changes in content and time of in-vitro scattering.

In-vivo pharmacokinetic studies of Flurbiprofen

Medication content in the plasma tests was evaluated utilizing the created HPLC technique. A standard chart was plotted to decide the medication by dissecting plasma tests containing various measures of medication. In the present examination blend of phosphate support (pH 3.5): acetonitrile (35:65) arrangement was utilized as the versatile stage.

Preparation of standard arrangements

Stock arrangement of 1mg/ml was set up by placing 100mg of medication into volumetric flagon (100ml) and 5ml of portable stage was included, sonicated and made the volume with same. From this 10ml stock course was taken into 100 ml volumetric container volume was made up to make 100µg/ml. From this 10 ml was taken and volume was made to 100 ml in volumetric container conveys 10µg / ml. From this 20 ml stock game plan, 100 ml volumetric container volume is made to distribute 2000ng / ml. From this, 1, 2, 3, 4, 5 and 6 ml stock solutions were taken to produce 200, 400, 600, 800, 1000 and 1200ng / ml standard solutions of Flurbiprofen to prepare the standard curve. FLB spiked plasma samples were prepared mixing with 0.5ml of blank plasma with above standard solutions. Plain plasma is used as the blank.

Extraction procedure

One ml of drug solution containing 200, 400, 600, 800, 1000 and 1200 ng/ml were combined to a series of test tubes containing 0.5ml of plasma. Then 0.5 ml acetonitrile was added to each tube and centrifuged at 3000rpm for 10min and injected each solution into HPLC to determine the peak area. Then standard curve was plotted between peak area and concentration and calculated slope and correlation coefficient.

Chromatographic conditions

The Chromatographic techniques were done on Shimadzu HPLC furnished with C_{18} segment and UV indicator. Portable stage was separated through 0.45µm film channel and pushed through the segment Symmetry C_{18} (X Terra, 4.6 x 150 mm) 5µm, at a stream pace of 1ml/min and run time was 10 min. Stock arrangement (1mg/ml) of FLB was readied utilizing the versatile stage. The section was equilibrated for 30 min and the dissected at 254nm utilizing an UV identifier.

Pharmacokinetic assessment in bunnies

The institutional creature moral board of trustees (IAEC) of Chaitanya College of Pharmacy Education and Research, Hanamkonda, Warangal concurred the proposed convention of bioavailability investigation of Rapid Disintegrating Tablets of Flurbiprofen. The endorsement was recorded and convention endorsement number was 02/IAEC/CCPER/CPCSEA/2017.

Subjects and study design

Twelve male light-skinned rabbits weighing 1.9 ± 0.2 kg were used for this evaluation. In the present assessment, a cross breed report was adopted in which twelve male pale cleaned individual bunnies were divided into two equal assemblies (Group I and Get-Together II). During prime time, group I (n = 6) chose the Power Tablet (50 mg isolate), however FF6 quickly separated the tablet (parcel 50 mg) to Pack II (n = 6). Those who fast for life have free access to water from twelve hours of evaluation. A forced measurement of water is added to surface tablet before being controlled. The mouth stopped for 2 minutes to swear chewing or gulping tablet. Two milliliters of water dose was administered as result. In the second period examination, following 35 days washout period, bunch I got FF6 quickly crumbling tablet and gathering II got control tablet. Blood tests were gathered at 0.125, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24h in the wake of dosing from peripheral vein.

HPLC analysis of Flurbiprofen plasma samples

The collected blood tests were centrifuged at 4000 rpm for 15 min with serum and transferred to 5ml downsized scale rotator tubes. 1ml of acetonitrile on serum was centrifuged at 3000 rpm for 10000 min, and the supernatant fluid was isolated at 40ºC until the assay test for immobilized solution [8].The HPLC technique has been used to calm serum stabilization. The quantitative validation drug in plasma was performed using the HPLC method by mixing supernatant liquid in HPLC section (circle volume 20 µl and stream rate 1 ml / min). Temperature run time was estimated by checking at 254nm for 10 minutes using a UV identifier.

Pharmacokinetic parameters

Pharmacokinetic parameters were solved using the Drug Scatter Plasma Stabilization Time information. Pharmacokinetic parameters were reviewed from plasma data for each subject using PK Solver (Change 2.0, Baylor College of Medicine, Houston, TX). From Plasma Focus vs. Plasma Focus, Pinnacle Plasma Fixation (Cmax) has the opportunity to connect at apex plasma levels (t_{max}).

RESULTS AND DISCUSSION

Solubility studies of Flurbiprofen

As Flurbiprofen is a class II drug. It was poorly solubilized in pH 6.0 and 6.8 pH buffer with increase in pH range solubility was increased it was easily solubilized in dichloromethane, acetone and methanol.

Compatibility considers

Medication similarity studies were done to know any conceivable communication of flurbiprofen with regular superdisintegrants and transporter utilized in plans utilizing Fourier transform infra red Spectroscopy and differential scanning colorimetry.

In the FT-IR studies shows that in the Flurbiprofen pure drug, Flurbiprofen and to pharmacopoeial specifications dehydrated banana powder, optimized solid dispersion (FS6) and optimized rapidly disintegrating tablet (FF6), there is no interaction drug with other excipients. FTIR spectrums were shown in figures 1, 2 and 3

DSC thermogram of Flurbiprofen shows a sharp endothermic peak at 113.4°C with normalized energy of 57.8 m J/mg, The thermogram of optimized solid dispersion FS6 showed two broad endotherms at 65.2°C and 116.2°C, with energies of 42.1m J/mg and 35.4 m J/mg respectively. Results reveal that there is no interaction between drug and PEG6000. DSC thermograms were shown in figures 5 and 6

Preformulation study

The results for characterization of blended powder are shown in table 3. The bulk density of blend varied between 0.303-0.326g/cm3. The tapped density was found in the range of 0.341-0.372 g/cm3. The powder blends of all formulations had Hausner's ratio of less than 1.25 indicating good flow characteristics, compressibility index less than 25% were considered as free flowing ones i.e. 9.1-14.7, the angle of repose below 35 degrees ranges indicates good flow properties i.e. 22.3-27.6. [5]

Dissolution studies of solid dispersions

When dissolution studies were conducted to solid dispersions and pure drug solid dispersion with 1:5 showed better dissolution rate when compared to other ratios solid dispersion and pure drug. The %CDR of drug was increased with the increase in the concentration of carrier concentration. But the decreased pattern was observed in FS6 solid dispersion due to retardant effect of PEG6000 with excess concentration. Dissolution profiles of solid dispersions was shown in figure 7

Evaluation of rapid disintegrating tablets of Flurbiprofen

All the tablets were white in color, round in shape with smooth surface without any defects. The diameter of all the formulations was uniform (7.7-7.8mm). Thickness of all the formulations was found to be within the range of 2.23mm to 2.53mm, all the formulations passed weight variation test as the % weight variation was within the pharmacopoeial limits of ± 7.5%, the hardness is in the range of 3.5-4.5kg/cm2, friability was observed less than1%, the wetting time was rapid in all the formulations the range of 24-33sec which is closely related to inner structure of tablets, in vitro disintegration time is in the range of 21.67-25.25 according to pharmacopoeial specifications banana powder when comes in contact with water they quickly wicks water into the tablet through capillary action to create internal pressure that disintegrate tablet, drug content was found within the range of 98.21-98.64 indicating uniform distribution of drug in all the formulated tablets as per pharmacopoeial specifications. Dissolution data of Flurbiprofen rapidly disintegrating tablets containing different superdisintegrants were shown in figures 8, 9 and 10.

Formulations containing Mango peel pectin as super disintegrant shown poor % CDR values when compared with other natural super disintegrants. Among mango peel pectin tablets, formulation FF4 8% showed maximum release of drug with 86% for 30 min. Increased concentration of mango peel pectin may increase the release of the drug with the wicking mechanism. Dehydrated banana powder showed maximum drug release when compared with the other formulations. Among these tablets, formulation FF6 4% showed maximum release of drug with 99% for 30 min. further increase in the concentration of the dehydrated banana powder retarded drug release in the subsequent increased concentrations FF8 6% and FF9 with the release of 70% and 80% respectively. Orange peel pectin as super disintegrant also shown poor %CDR values when compared with other natural super disintegrants. Among Orange peel pectin tablets, formulation FF12 8% showed maximum release of drug with 83% for 30 min at the concentration 2% drug release was 86% only. These studies suggested that increased concentration of orange peel pectin may increase the release of the drug with the wicking mechanism and burst release mechanism.

Among all the formulations dehydrated banana powder containing formulations FF4 and FF6 shown to better release rate of flurbiprofen from the dosage form. Thus dehydrated banana powder can use as better natural superdisintegrant in development rapidly disintegrating tablets.

Stability studies of optimized formulation FF6

Strength investigations of the plan FF6 of quickly deteriorating tablets were completed to decide the impact of definition added substances on the steadiness of the medication and furthermore to decide the physical dependability of the detailing. The soundness studies were conveyed at 45±1ºC for 90 days. Medication content during the examination time frame.

In-vivo pharmacokinetic Studies

Analytical method development: HPLC method

The HPLC method was developed total run time was set to 10min and chromatograms of Flurbiprofen appeared at 3.907 min. The chromatograms of blank plasma, pure Flurbiprofen in plasma and Flurbiprofen in mobile phase were shown in figure 11, 12 and 13. The peak area of Flurbiprofen in mobile phase and plasma was almost similar that indicating.

Pharmacokinetic evaluation in rabbits

In this design, pharmacokinetic evaluation was done on rapidly disintegrating tablets FF6 in comparison to control tablet of Flurbiprofen. The *in vitro* data comparison between control and fast dissolving tablets were given in figure 14.

This part of the study interprets in vivo pharmacokinetic investigations of FF6 solid dispersion of Flurbiprofen to verify enhancement dissolution and absorption rate when contrasted to pure drug. The objective in vivo pharmacokinetic investigations was to recount the time course of Flurbiprofen concentrations in blood.

From the pharmacokinetic assessment, Flurbiprofen showed up very quickly inside 10 min. in plasma. Increased worth of Ka was observed in FF6 when compared to control tablet that shows the enhanced absorption rate. The $t_{1/2}$ was found as 5.13 and 5.18 hr for control and FF6 tablets respectively. The solid dispersion reached peak concentration (C_{max}) 11445.46 ng/ml at t_{max} of 2 h while it was seen event of control tablet, showing that upgrade of retention in strong scattering example of flurbiprofen than unadulterated structure. The AUC of control and FF6 tablets of flurbiprofen were 31495.16 and 43126.52 ng-h/ml correspondingly. These outcomes demonstrated that the FF6 tablet indicated improvement of AUC when contrasted with control tablet of flurbiprofen. The MRT of control and FF6 quickly breaking down tablets were 5.58 h and 6.00 h individually.

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The factual examination of pharmacokinetic parameters of control and FF6 quickly was breaking down critical distinction in the ka among control and FF6 quickly deteriorating tablets, demonstrating that the pace of assimilation is more if there should arises an occurrence of FF6. There was a noteworthy contrast of AUC0-∞ saw among control and FF6 tablets, which demonstrate the improvement of degree of retention of Flurbiprofen.

The C_{max} and t_{max} of control and FF6 rapidly disintegrating tablets were significantly different indicating immediate absorption of Flurbiprofen from FF6 tablets. Significant difference of MRT between control and FF6 rapidly disintegrating tablets indicated that difference in time spent by the Flurbiprofen in the body.

All in all, the FF6 quickly breaking down tablets indicated brisk and complete medication discharge inside 30 min. contrasted with control tablets that brought about early tmax and higher Cmax. As needs be the consequences of the pharmacokinetic study uncovered that the FF6 quickly crumbling tablets containing PEG600 strong scattering improves the bioavailability of inadequately solvent flurbiprofen.

Table 2: Formulae of Rapidly Disintegrating Tablets of Flurbiprofen with Natural Superdisintegrants

S.No	Ingredients (mg)	FF1	FF2	FF3	FF4	FF5	FF6	FF7	FF8	FF9	FF10	FF11	FF12
1	Flurbiprofen FS6 (Solid dispersion equivalent to 50 mg of Pure drug)	300	300	300	300	300	300	300	300	300	300	300	300
2	MCC PH 102	q.s	q.s	q.s	q.s.	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
3	Mannitol	35	35	35	35	35	35	35	35	35	35	35	35
4	Mango peel pectin	9	18	27	36	_	_	_	_	_	_	_	_
5	Banana powder	_	_	_	_	9	18	27	36	_	_	_	_
6	Orange peel pectin	_	_	_	_	_	_	_	_	9	18	27	36
7	Aspartame	6	6	6	6	6	6	6	6	6	6	6	6
8	Magnesium stearate	6	6	6	6	6	6	6	6	6	6	6	6
9	Talc	3	3	3	3	3	3	3	3	3	3	3	3
	Total Tablet Weight	**450**	**450**	**450**	**450**	**450**	**450**	**450**	**450**	**450**	**450**	**450**	**450**

Table 3: Pre compression results of formulations FF1-FF12

Formulae	Angle of Repose (θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	HR ratio	Carr's Index
FF1	23.67 ±1.15	0.324±0.008	0.366 ±0.012	1.129	11.4
FF2	22.3 ±1.52	0.326±0.031	0.359 ±0.031	1.101	9.1
FF3	23 ±1.00	0.317±0.010	0.372 ±0.026	1.173	14.7
FF4	27.67±1.52	0.312 ± 0.01	0.355 ±0.010	1.137	12.1
FF5	25.67 ±1.15	0.309±0.0018	0.341 ±0.176	1.103	9.3
FF6	25.33 ±2.08	0.303±0.014	0.349 ± 0.014	1.151	13.1
FF7	23.33 ±1.52	0.318±0.005	0.354 ±0.011	1.113	10.1
FF8	27 ±1.73	0.309±0.006	0.381 ±0.022	1.249	12.8
FF9	27.33 ±1.52	0.305±0.007	0.375 ±0.012	1.229	13.8
FF10	21.33 ±2.08	0.316±0.006	0.377 ± 0.020	1.193	14.2
FF11	22.33 ±2.51	0.305±0.016	0.378 ±0.012	1.239	11.4
FF12	22.67±2.51	0.316±0.006	0.390 ±0.003	1.234	14.9

Table 4: Post compression parameters of Rapidly Disintegrating Tablets of Flurbiprofen

Formulae	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content	Wetting time(sec)	Water absorption ratio	*In-vitro* Disintegration (sec)
FF1	450.1±1.619	3.08±0.209	3.13±0.205	0.50±0.020	98.57±0.157	24.00±2.00	36.00±2.00	21.67 ±1.52
FF2	450.3±2.336	3.09±0.314	3.18±0.044	0.51±0.025	98.64±0.332	27.67±1.52	39.00 ±4.00	20.66 ±1.52
FF3	449.1±2.458	3.08±0.265	3.18±0.265	0.46±0.041	98.21±0.340	25.33±2.64	35.00 ±2.00	22.33 ±2.00
FF4	449.3±2.131	2.99±0.288	3.19±0.265	0.48±0.025	99.03±0.468	33.00±4.04	45.00 ±4.00	25.25 ±2.00
FF5	449.7±2.846	3.06±0.189	3.16±0.245	0.48±0.025	98.29±0.605	30.00±1.00	55.30±2.56	23.35 ±2.523
FF6	450.6±2.549	3.00±0.200	3.14±0.313	0.50±0.030	98.92±0.824	35.00±3.00	39.30 ±3.51	26.33 ±1.52
FF7	450.1±2.213	3.04±0.177	3.18±0.252	0.40±0.015	98.94±0.703	20.00±2.00	42.00 ±2.00	32.54 ±1.00
FF8	448.9±1.494	3.05±0.190	3.09±0.223	0.39±0.026	98.13±0.460	22.67±3.50	39.00 ±2.51	30.33 ±2.00
FF9	450.2±1.897	3.02±0.214	3.08±0.229	0.43±0.020	99.54±0.860	25.33±1.52	44.00 ±3.78	34.35 ±2.00
FF10	450.5±1.032	2.98±0.154	3.15±0.246	0.48±0.020	99.22±0.393	21.00±3.00	69.67 ±2.00	36.15 ±2.08
FF11	450.8±1.686	3.00±0.188	3.13±0.226	0.5±0.0170	98.87±0.363	18.00±2.00	71.33 ±4.16	35.65 ±1.52
FF12	450.3±1.414	3.03±0.188	3.2 ±0.249	0.49±0.015	99.95±0.836	22.00±2.00	65.00 ±3.60	38.14 ±2.00

Table 5: Drug content data of stability formulation (FF6)

Trial no	1st day	30th day	90th day
I	99.27	94.37	97.39
II	99.27	94.37	97.39
III	99.17	90.23	93.75
Mean(X)	98.55	90.30	93.11
SD	0.298	0.210	0.515

*Average of three determinations

Table 6: Pharmacokinetic parameters of Flurbiprofen control and FF6 rapidly disintegrating tablets (Mean±S.D, n=12)

Parameters	Control tablet	FF6 RDTs	*t*-test at 0.05 LS
ka (1/h)	0.402±0.01	0.486±0.01	Significant
ke (1/h)	0.135±0.01	0.134±0.01	Not Significant
$t_{1/2}$ (h)	5.13±1.25	5.18±1.52	Not Significant
T_{max} (h)	3.00±0.01	2.00±0.01	Significant
C_{max} (ng/ml)	9140.84±614.36	11445.46±149.23	Significant
$AUC_{0-\infty}$(ng- h /ml)	31495.16±619.92	43126.52±688.89	Significant
$AUMC_{0-\infty}$(ng-h^2/ml)	175957.60±3046.49	258895.00±3103.94	Significant
MRT (h)	5.58±0.03	6.00±0.03	Significant

Figure1: FTIR spectrum of Flurbiprofen pure drug

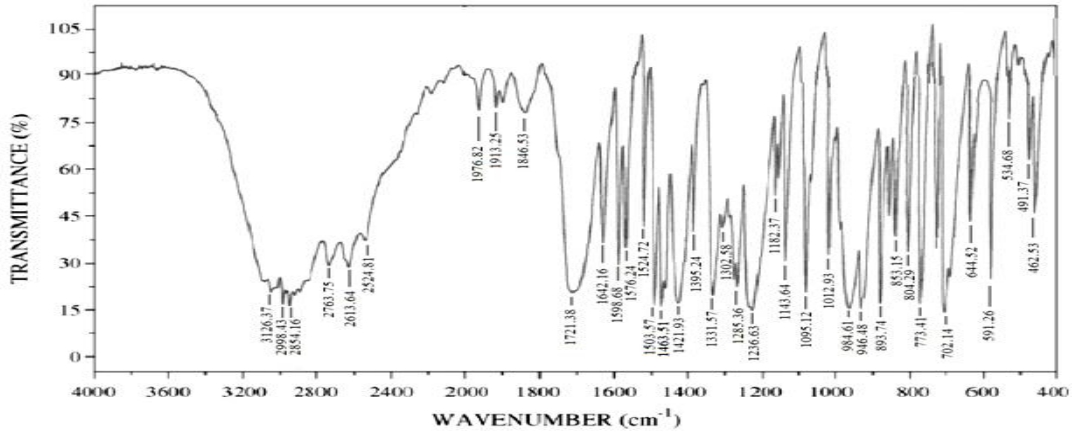

Figure 2: FTIR spectrum of Physical mixture containing Flurbiprofen and Dehydrated banana powder

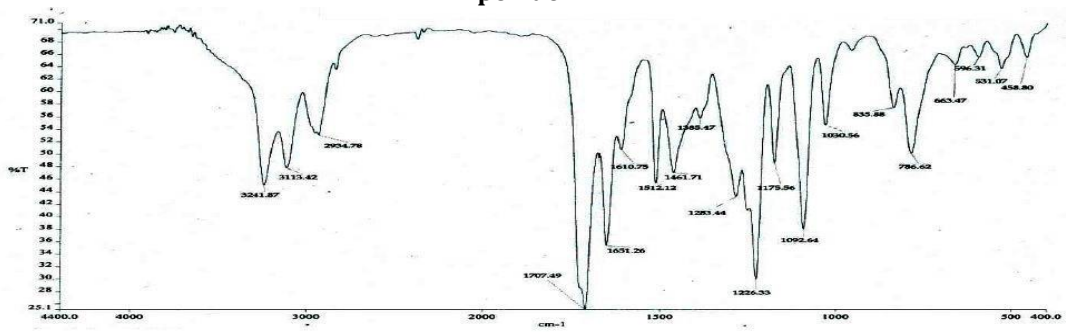

Figure 3: FTIR spectrum of Best solid dispersion FS6

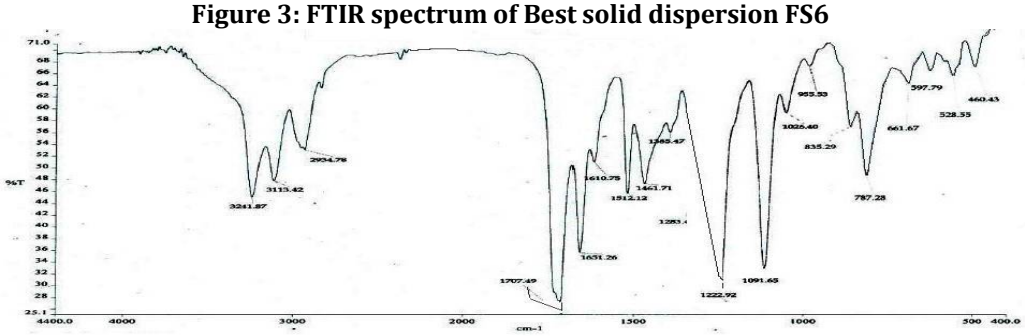

Figure 4: FTIR spectrum of Best formulation FF6

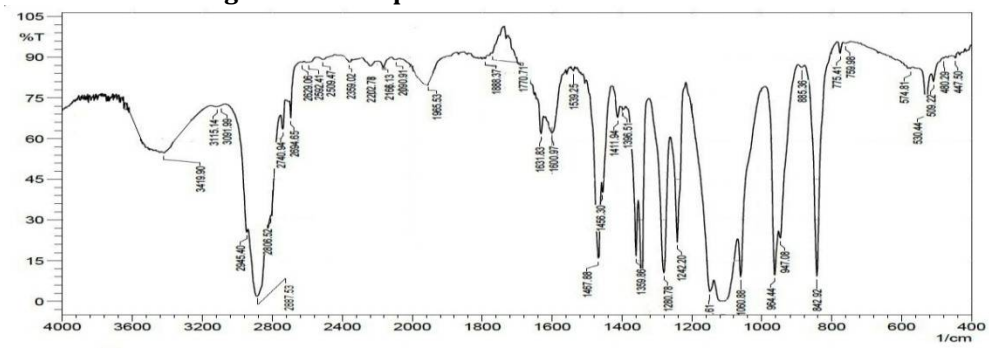

Figure 5: DSC thermogram of Flurbiprofen pure drug

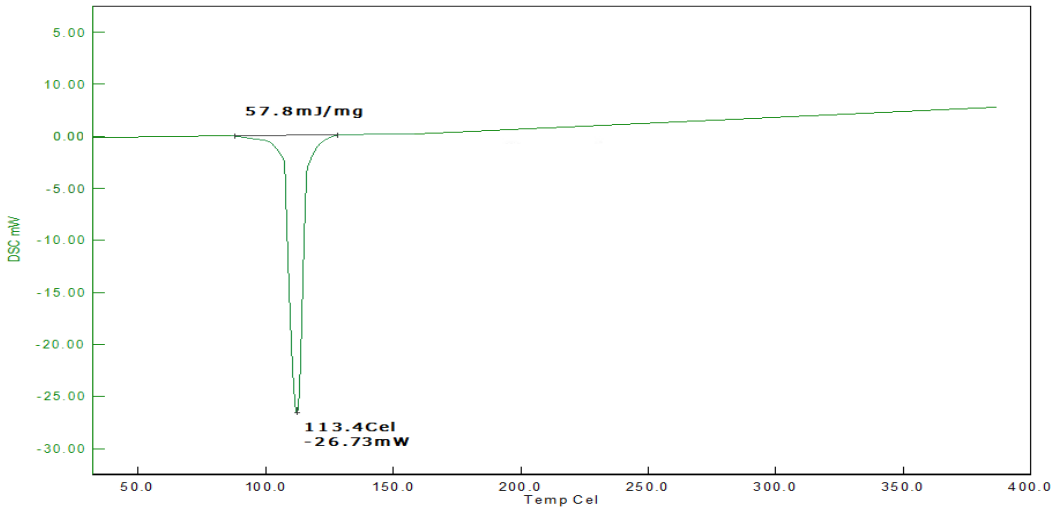

Figure 6: DSC thermogram of Flurbiprofen-PEG 6000 solid dispersion

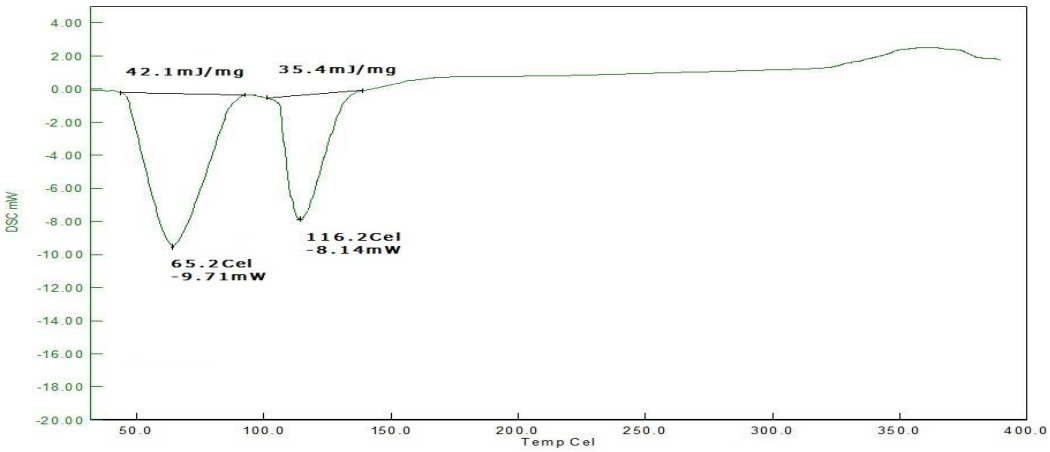

Figure 7: Dissolution profiles (%CDR) of solid dispersions

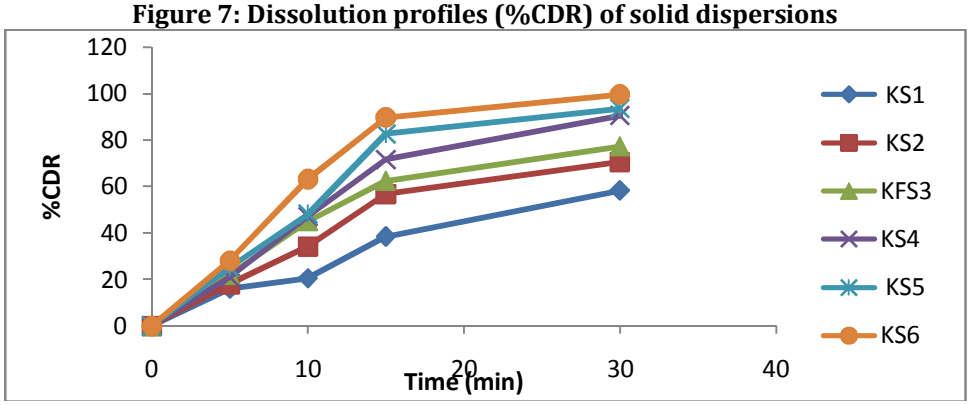

Figure 8: Dissolution data of Flurbiprofen rapidly disintegrating tablets containing Mango peel pectin

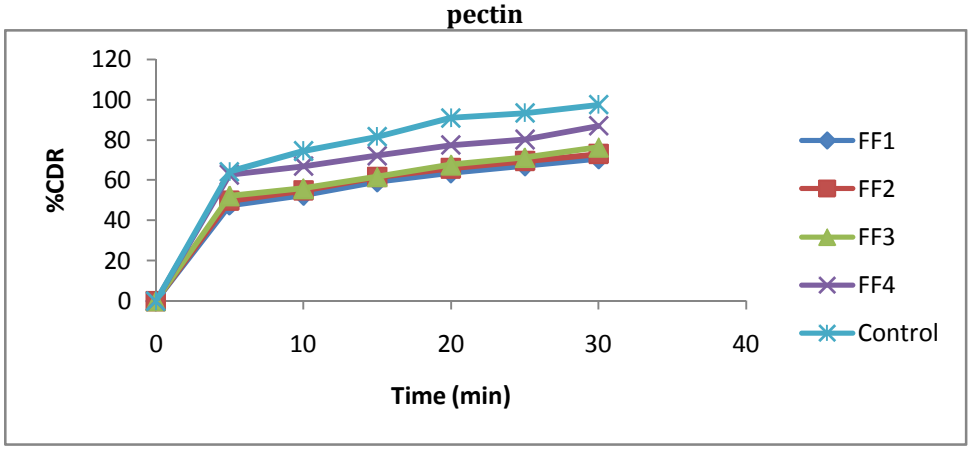

Figure 9: Dissolution data of Flurbiprofen rapidly disintegrating tablets containing dehydrated banana powder

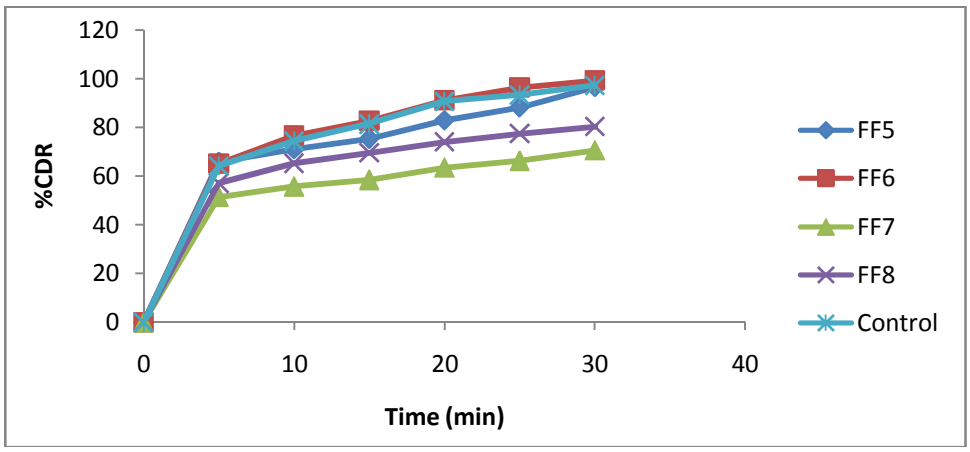

Figure 10: Dissolution data of Flurbiprofen rapidly disintegrating tablets containing orange peel pectin

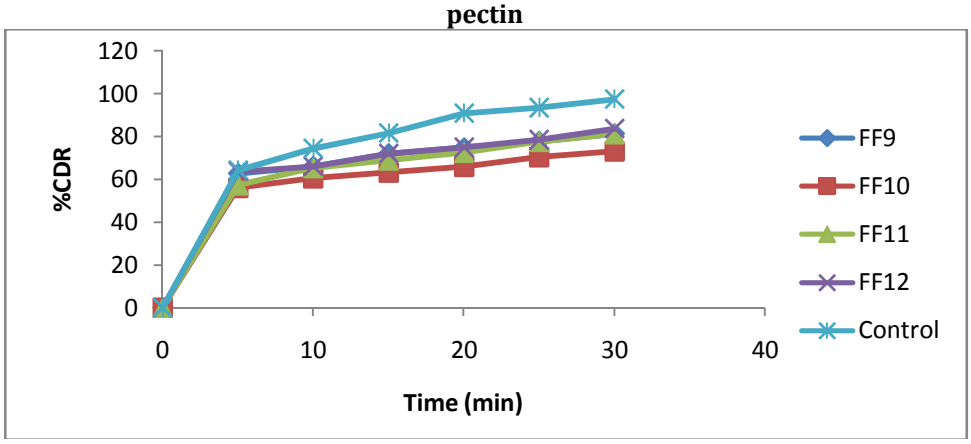

Figure 11: Chromatogram of blank plasma

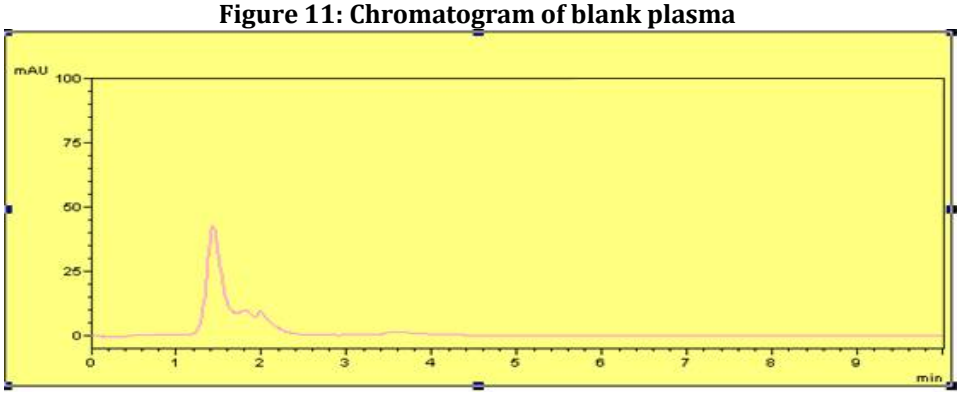

Figure 12: Chromatogram of pure Flurbiprofen in plasma

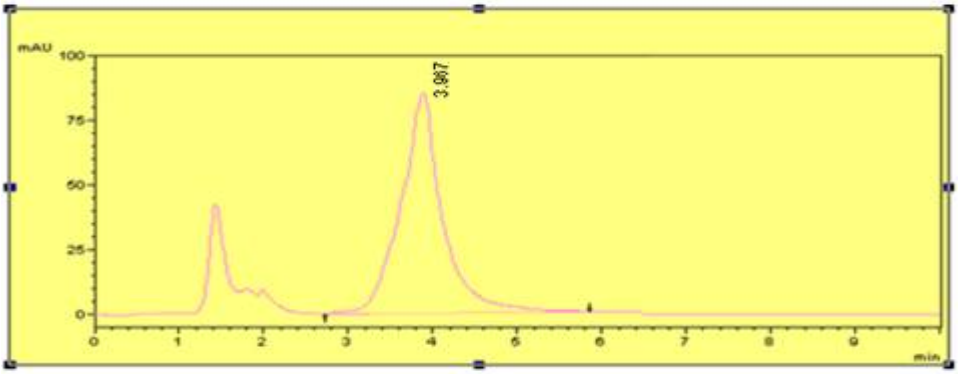

Figure 13: Chromatogram of Flurbiprofen in mobile phase

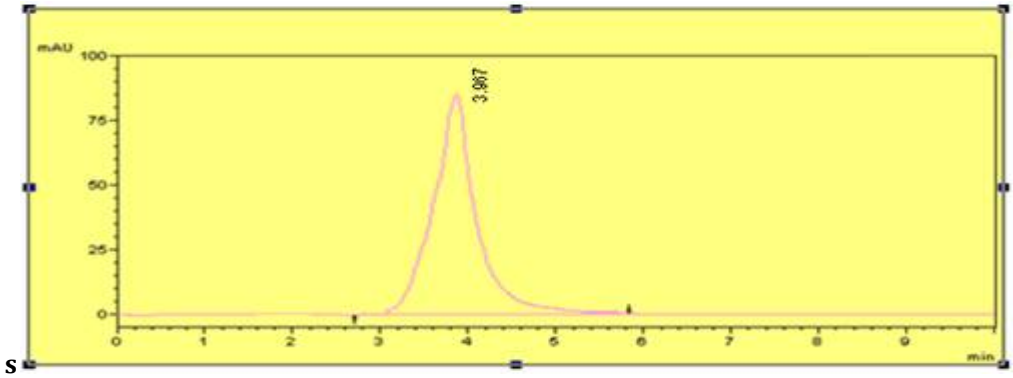

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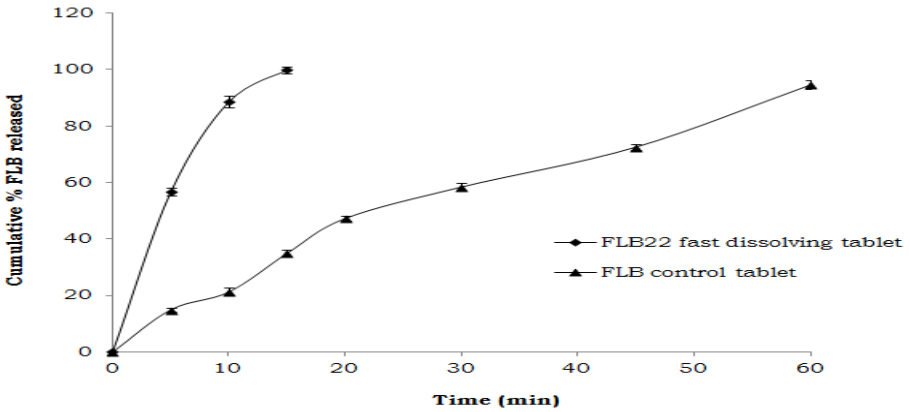
Figure 14: *In vitro* Flurbiprofen release from control and optimized formulation (n=3)



CONCLUSION

The results was obtained from the study, flurbiprofen solid dispersions were prepared by using PEG6000 as carrier, flurbiprofen fast disintegrating tablets were prepared by direct compression method by using optimized flurbiprofen solid dispersion with Mango peel pectin, dehydrated banana powder and Orange peel pectin as super disintegrants. All the formulations showed fast disintegrating action. Among all the formulations dehydrated banana powder containing formulations FF5 and FF6 showed less disintegration time and better release rate of flurbiprofen from the dosage form within thirty minutes. Thus, dehydrated banana powder can be utilized as better regular superdisintegrant in the advancement of quickly breaking down tablets when compared to orange peel pectin and mango peel pectin. The conclusion of design and development of fast disintegrating tablets of flurbiprofen can defeat the inconvenience of poor and off beat oral bioavailability of flurbiprofen related with current advanced oral specifying. Further move in direction of this way is required so as help it adequacy by pharmacokinetic and pharmacodynamic thinks about in individuals.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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