FORMULATION AND EVALUATION OF FLURBIPROFEN FAST DISINTEGRATING TABLETS USING NATURAL SUPERDISINTEGRANTS

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ABSTRACT

Objective: The main objective of this research was to formulate the fast disintegrating tablets (FDT’s) of flurbiprofen incorporating superdisintegrants, isolated from natural sources such as Plantago ovata (PO) seeds, Lepidium sativum (LS) seeds, and agar-agar (malt agar).

Methods: Superdisintegrants were isolated from their natural sources using reported methods. Swelling index and hydration capacity were determined for the natural superdisintegrants to know their disintegration capacity. The tablet formulations were designed using isolated natural superdisintegrants. The powder blends were evaluated for pre-compression parameters such as angle of repose, bulk density, tapped density, Carr’s index, and Hausner’s ratio. FDT’s were prepared by direct compression method. The compressed tablets were characterized for post-compression parameters.

Results: All formulations had hardness, friability, weight variation, and drug content within the pharmacopoeial limits. The wetting time was 84-254 seconds, in vitro disintegration time was between 59.2 and 221 seconds, and in vitro drug release was as low as LS1 - 11.80% to a maximum of PO4 - 98.99% after 4 minutes of study. Among all, optimized formulation was PO4, as it showed good wetting time 94 seconds, fastest disintegration time 59.2 seconds, dispersion time 135 seconds, and drug release of 98.99% within 4 minutes.

Conclusion: Flurbiprofen FDT’s were successfully developed using isolated natural disintegrants. The natural disintegrants isolated showed promising results and can prove as effective alternative for synthetic disintegrants.

Keywords: Flurbiprofen, Fast disintegrating tablets, Plantago ovata, Lepidium sativum, Agar-agar.

INTRODUCTION

Fast disintegrating tablets (FDT’s) 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. FDT’s are not only useful in administration of drugs in pediatric and geriatric patients but also in patients suffering from dysphasia and are ideal for active people as well [1,2]. These dosage forms show good stability, ease of manufacture, and ease of handling by patients. Flurbiprofen is a poor water soluble drug (pKa=4.42) that is available in the market as a non-steroidal anti-inflammatory agent [3]. It is primarily intended to treat painful conditions, which requires fast release of the drug [4]. Flurbiprofen is Class II drug and is absorbed at a slower rate from oral route and dissolution rate is the rate limiting step [5]. This makes it difficult for absorption and thereby bioavailability of drug. In the present study, our efforts are toward making a FDT’s of flurbiprofen that can increase its solubility and dissolution rate and hence bioavailability of drug. Some of the recent research examples for flurbiprofen fast dissolving systems are flurbiprofen fast dissolving tablets [6], flurbiprofen fast dissolving tablets [7], and flurbiprofen solid dispersions [8]. It is observed that in most of the research works direct compression is widely used for preparing FDT’s. Direct compression is one of the techniques which require incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration [9,10]. FDT’s can be prepared using two types of superdisintegrants; natural and synthetic. Compared to synthetic fast tablet disintegration [9,10]. FDT’s can be prepared using two types of superdisintegrants; natural and synthetic. Hence, in the present research, it was aimed to prepare novel flurbiprofen FDT’s using natural superdisintegrants, which can increase the solubility and dissolution of the drug and also is safe.

MATERIALS AND METHODS

Flurbiprofen was obtained as a gift sample from FDC Limited, Mumbai, India. Plantago ovata (PO) and Lepidium sativum (LS) seeds were purchased from local market, Raichur, India. Spray dried mannitol was procured from SPI Pharma, agar-agar, and microbial culture collection were purchased from 5D Fine Chemicals Pvt. Ltd., Mumbai, India. Aemisl 200 was obtained from HiMedia Laboratories Pvt. Ltd., Mumbai, India. All other chemicals and reagents used were of pharmaceutical and analytical grade.

Isolation of mucilage from PO seeds
PO seeds (Fig. 1) were soaked in distilled water for 48 hrs and again some more amount of water was added, kept for next 48 hrs. Later it was boiled for few minutes for complete release of mucilage into water. The material was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate, so as to precipitate the mucilage. The separated mucilage was dried in oven at temperature <60°C, powdered, sieved (#80), and stored in a desiccator until use [12].

Isolation of mucilage from LS seeds
LS seeds (Fig. 2) contain the mucilage around the outer layer. Mucilage was extracted by soaking the seeds with 10 times of its weight with distilled water and kept for 24 hrs. The viscous solution obtained was passed through 8-folds of muslin cloth. Then, the mucilage was precipitated well by addition of 95% ethanol in the ratio 1:1 by constant stirring. The coagulated mass was dried in an oven at 40-45°C till it was completely dried. The dried powders were grinding with mortar and pestle. The powder was passed through 80 mesh (#) and stored in a desiccator [13].

Preparation of modified agar
Suitable quantity of agar powder (Fig. 3) (5-10 g) is weighed and added in distilled water (100 ml). Agitation is done continuously by magnetic
stirrer for 24 hrs to swell. The swollen contents are dried on a tray for three-dimensions at room temperature. The dried powders are ground by mortar and pestle and passed through 80 mesh (#) and stored in desiccator [14].

Characterization of dried isolated mucilages/prepared natural super disintegrants

Swelling index (SI) of superdisintegrants

The isolated/prepared natural superdisintegrants (1 g) were taken in separate measuring cylinders. Then, distilled water (100 ml) was poured in them separately. The measuring cylinder was shaken vigorously for 10 minutes and allowed to stand for 24 hrs at 37±0.5°C. The experiment was carried out in triplicate and mean was taken.

Swelling capacity was expressed as percentage and calculated using following formula:

Swelling capacity (%) = \( \frac{X_v}{X_i} \times 100 \)

Where,

\( X_v \) = Final volume occupied by swollen material after 24 hrs.

\( X_i \) = Initial volume occupied by powder in measuring cylinder.

SI (%) = \( \frac{\text{Final volume} - \text{Initial volume}}{\text{Initial volume}} \times 100 \)

The swollen mass from measuring cylinder, at the end of test period was removed and weighed (g) to get the final weight and percentage increase in weight was determined by using the following equation.

Increase in weight (%) = \( \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100 \)

Percentage increase in weight was used to interpret water uptake capacity of the supersedintegrants [15].

Hydration capacity (HC) of superdisintegrants

The isolated/prepared natural superdisintegrants (1 g) were taken in the three different 15 ml tarred centrifuge tubes. Then, 10 ml of distilled water was added to each centrifuge tube and allowed to centrifuge for 2 hrs at 3000 rpm. After the centrifugation process, the tarred centrifuge tube was taken out and inverted to remove the supernatant liquid [16]. The decanted tube then weighed on digital balance and the HC was calculated using the following equation.

\[ \text{HC} = \frac{\text{Weight of hydrate sample}}{\text{Weight of dry sample}} \]

The experiment was carried out in triplicate and mean was taken.

Preformulation studies

Fourier transform infrared spectroscopy (FT-IR) study

The compatibility between pure drug and excipients was detected by FT-IR spectra obtained on comp-Bruker, model alpha-T, (USA). The pellets were prepared on KBr press. The spectra were recorded over the wave number range of 4000-500 cm\(^{-1}\) for pure flurbiprofen and 3500-500 cm\(^{-1}\) for flurbiprofen FDT.

Differential scanning calorimeter (DSC) studies

Thermograms of pure flurbiprofen and its formulation were obtained by using DSC (Mettler Star SW 8.10) at a heating rate 10°C/minutes over a temperature range of 35-300°C. Accurately weighed 2.0 mg of the sample was hermetically sealed in an aluminum pan. Nitrogen gas was purged at rate of 10 ml/minutes for maintaining inert atmosphere.

Preparation of flurbiprofen FDT’s

FDT’s of flurbiprofen were prepared using direct compression method. All the ingredients were taken in sufficient quantity and passed through sieve number 80. The natural superdisintegrants PO, LS and modified agar were used in concentrations of 2%, 4%, 6%, and 8% to formulate the tablets. All the ingredients as shown in Table 1 were co-ground in a pestle and mortar and then magnesium stearate and talc were added and mixed for 10 minutes. The mixed blend of drug excipients was compressed using 10 stations compression machine to produce tablets.

Pre-compression evaluation of flurbiprofen FDT formulations

Angle of repose

The angle of repose (\( \alpha \)) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (\( H \)) was obtained. The radius of the heap (\( r \)) was measured and angle of repose was calculated [17]. \( \alpha = \tan^{-1} \frac{H}{r} \). The experiment was carried out in triplicate and mean±standard deviation (SD) values were taken.

Bulk density

Apparent bulk density (\( \rho_b \)) was determined by placing perceived drug excipients blend in to a graduated cylinder and measuring the volume (\( V_b \)) and weight (\( M_b \)) as it is. \( \rho_b = \frac{M_b}{V_b} \).

Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (\( V_t \)) occupied in the cylinder and weight (\( M_t \)) of the blend was measured [18]. The tapped density (\( \rho_t \)) was calculated using the following formula:

\[ \rho_t = \frac{M_t}{V_t} \]

The experiment was carried out in triplicate and mean±SD values were taken.
were calculated. The procedure was repeated thrice, and the mean±SD values determined. The resulting dispersion was passed through sieve number

One tablet was placed in a beaker containing 100 ml of pH 6.8 phosphate buffer at 37±0.5°C and the time required for complete dispersion was compared with that of average weight and the amount of weight variation was determined [22].

Friability test was performed by using Roche friabilator. 10 tablets from each formulation were randomly selected and the average of applied pressure (kg/cm²) for crushing the tablet was determined [20]. From the average, SD values was calculated. The result was expressed in millimeter.

Hardness

Hardness was determined by using a Pfizer hardness tester, taking 10 tablets from each formulation, and the average of applied pressure (kg/cm²) for crushing the tablet was determined [20]. From the average, SD values was calculated.

Friability

Friability test was performed by using Roche friabilator. 10 tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions/minutes (rpm). After 4 minutes (100 rpm), the tablets were deducted and reweighed. The percentage friability was determined [21]. The test was performed thrice, and the mean±SD values were calculated.

Weight variation

About 20 tablets were randomly selected and individually weighed. The average weight of tablets was calculated. Then, the individual weight was compared with that of average weight and the amount of weight variation was determined [22].

Dispersion time

One tablet was placed in a beaker containing 100 ml of pH 6.8 phosphate buffer at 37±0.5°C and the time required for complete dispersion was determined. The resulting dispersion was passed through sieve number 22 [23]. The procedure was repeated thrice, and the mean±SD values were calculated.

**ResulTs and Discussion**

Isolation of the mucilages/natural superdisintegrants was carried out from PO seeds, LS seeds, and agar-agar. The obtained dried powders were tested for SI and HC. The results are given in Figs. 4 and 5.

Superdisintegrants are generally used at low level, typically 1-10% by weight relative to the total weight of the dosage unit. Swelling and HC are the important parameters for comparing disintegration efficiency.

Table 1: Composition of flurbiprofen fast disintegrating tablets

| Ingredients          | PO1 (mg) | PO2 (mg) | PO3 (mg) | PO4 (mg) | LS1 (mg) | LS2 (mg) | LS3 (mg) | LS4 (mg) | MA1 (mg) | MA2 (mg) | MA3 (mg) | MA4 (mg) |
|----------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Flurbiprofen         | 50       | 50       | 50       | 50       | 50       | 50       | 50       | 50       | 50       | 50       | 50       | 50       |
| Microcrystalline cellulose | 101      | 101      | 101      | 101      | 101      | 101      | 101      | 101      | 101      | 101      | 101      | 101      |
| Spray dried mannitol | 40       | 36       | 32       | 28       | 40       | 36       | 32       | 28       | 40       | 36       | 32       | 28       |
| Plantago ovata       | 4        | 8        | 12       | 16       | -        | -        | -        | -        | -        | -        | -        | -        |
| Lepidium sativum     | -        | -        | -        | -        | 4        | 8        | 12       | 16       | -        | -        | -        | -        |
| Modified agar        | -        | -        | -        | -        | -        | -        | -        | -        | 4        | 8        | 12       | 16       |
| Aerosil 200          | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        | 1        |
| Magnesium stearate   | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        |
| Talc                 | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        | 2        |

PO1-PO4, LS1-LS4, MA1-MA4 are formulation codes

**Drug content**

For estimation of drug content, 10 tablets were crushed, and the aliquot of powder equivalent to 50 mg of drug was extracted in methanol/phosphate buffer pH 6.8, suitably diluted using phosphate buffer pH 6.8 and determined by ultraviolet-visible spectrophotometer at 247 nm. Three powder samples were used to determine drug content, and the mean was derived from them. The drug content was calculated from the calibration curve [24].

**Wetting time**

A piece of tissue paper (12 × 10.75 cm) folded twice was placed in a Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting of tablet was noted. Three tablets from each formulation were randomly selected and the average wetting time in s was noted.

**Water absorption ratio**

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio was determined [25]. The test was performed thrice and mean was calculated.

**In vitro disintegration time**

The test was carried out in a disintegration test apparatus using distilled water as disintegration medium at 37±0.5°C. A tablet was placed in each of six tubes of the apparatus and one disc was added to each tube. The time taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured.

**In vitro dissolution study**

In vitro dissolution study was carried out using USP apparatus Type II (Paddle type). The dissolution medium used was pH 6.8 phosphate buffer (900 ml) maintained at temperature 37±0.5°C at 75 rpm. About 5 ml sample was withdrawn periodically and replaced with same volume of fresh medium. Absorbance of the solution was measured at 247 nm [26].

**Stability study**

The Stability study of flurbiprofen FDT PO4 was carried out at 40±2°C/75±5% RH for 6 month by storing in stability chamber and analyzed periodically at intervals of 1 month.

**RESULTS AND DISCUSSION**

Isolation of the mucilages/natural superdisintegrants was carried out from PO seeds, LS seeds, and agar-agar. The obtained dried powders were tested for SI and HC. The results are given in Figs. 4 and 5.

Superdisintegrants are generally used at low level, typically 1-10% by weight relative to the total weight of the dosage unit. Swelling and HC are the important parameters for comparing disintegration efficiency.
Generally, it is considered that higher the swelling and HC better the disintegration. PO was found to have higher SI and HC as it swells to a large extent in contact with water. In this study, it was observed that SI of PO was found higher than LS and malt agar (MA). PO because of its gelling and viscous property has higher SI than other disintegrants. The order of SI and HC was PO>LS>MA.

**Preformulation studies**

**FT-IR spectral study**

The comparative FT-IR spectral study of pure drug and formulation PO4 (drug with excipients) reveals the fact that there is no marked shift in the position of characteristic absorption band of the functional group and bonds present in the drug molecule. Hence, it may be concluded that there is no interaction of the drug with natural excipients. Figs. 6 and 7 represent the FT-IR spectra of pure drug and formulation PO4.

**DSC studies**

The thermograms revealed no significant change in the nature and height of the peak of drug molecule in both the graphs, suggesting that the drug has remained in its normal form without undergoing any interaction with natural excipients. Hence, it was concluded that there is no interaction of the drug with excipients of formulation. Figs. 8 and 9 represent the DSC thermograms of pure drug and formulation PO4, respectively.

**Precompression evaluation of flurbiprofen FDT powder blend**

For each formulation, blend of drug and excipients were evaluated for micromeritic properties. Angle of repose was found to be in the range of 25.03±0.16-37.30±0.24. The bulk density was found to be between 0.32±0.06 and 0.33±0.0.20 g/cm³ and tapped density between 0.39±0.44 and 0.41±0.08 g/cm³ for all formulations. From density data, Carr’s index was calculated and was found to be between 15.38%±0.14% and 21.22%±0.26%. Hausner ratio was found below 1.18±0.06. All the parameters showed good flow, compression, and blend properties for direct compression and hence tablets were prepared by direct compression method.

**Post-compression evaluation of flurbiprofen FDT’s**

The post-compression evaluation of flurbiprofen FDT’s is given in Tables 2 and 3.

The post-compression evaluation was carried out for all 12 formulations developed. It was observed that the thickness of tablets was found in the range of 4.62±0.90-4.88±0.78 mm. Diameter of all tablets was between 7.00±0.65 and 7.10±0.44 mm. The hardness of the prepared tablets was maintained within the range of 4.20±1.41-5.84±0.58 kg/cm²; it was considered adequate for mechanical stability, while manufacturing and handling the dosage form. The friability of all formulations was found to be <1% and was in the range of 0.07±0.45-0.45±1.22% indicating a good mechanical strength of tablets. The average weight of all compressed tablets was in the range 190±196 mg. All the tablets passed weight variation test as the % deviation was <7.5% as allowed in the pharmacopoeia [27]. The dispersion time is used as an indication for the ease of tablet disintegration. It was found in the range of 2.25±1.88-35.7±1.74 minutes. The drug content uniformity was in the range of 97.6±1.64-99.8±0.81%.

Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of fast disintegrating tablets [28]. Wetting time is closely related to the inner structure of the tablet. The wetting time was in between 84±1.74 and 650±2.49 seconds for all FDTs. It was observed that the wetting time was least for formulations prepared with PO and highest with LS formulations (Fig. 10). Promising formulation PO4 showed a wetting time of 84 seconds, which facilitates faster dispersion of tablet in mouth. The wetting time decreased with increasing superdisintegrant concentration for all the superdisintegrants used. The wetting times of tablets were in the order of PO<MA<LS.

**In vitro disintegration time**

The in vitro disintegration time was measured by the time taken by the FDT’s to undergo complete disintegration. The FDT’s prepared with PO PO1-PO4 disintegrated in 92.83±0.71, 68.2±0.96, 62.67±1.04, and 59.17±1.08 seconds, respectively. The FDT’s prepared with LS LS1-LS4, disintegrated in 221.7±1.24, 209±1.36, 172.8±0.74, and 122.5±0.94 seconds, respectively, whereas FDT’s with modified agar MA1-MA4 disintegrated in 109±1.54, 91.33±1.84, 72±1.98, and 61.67±2.34 seconds (Fig. 10). Formulations PO4 showed rapid disintegration compared to other formulations. The faster disintegration of tablets with PO is due to easy swelling ability and pronounced

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**Fig. 4:** Swelling index of natural superdisintegrants. The data represent mean of three determinations

**Fig. 5:** Hydration capacity of natural superdisintegrants. The data represent mean of three determinations

**Fig. 6:** Fourier transform infrared spectroscopy of pure flurbiprofen drug
The FDT’s with LS disintegrated rather slowly. This might be due to LS gelling nature. The water absorption and wetting of tablet takes more time because of its relatively high viscosity and pseudoplasticity. MA consists of two polysaccharides as agarose and agaropectin. Agarose is responsible for gel strength and Agaropectin is responsible for the viscosity of agar solutions [31]. The tablets with
MA disintegrated faster than LS. Comparatively, the disintegration times of tablets were in the order of PO < MA < LS. The results of in vitro disintegration time were in accordance with wetting time studies. It is interesting to note that though LS is having higher swelling and HC than MA; its wetting time is less compared to MA because it is more viscous and jelly than MA. It was observed that as the concentration of superdisintegrants increased from 2% to 5% w/w, the disintegration time reduced considerably. It was observed that all formulations satisfied the disintegration time criteria of fast dissolving tablets.

Water absorption ratio, which is important criteria for understanding the capacity of disintegrants to swell in the presence of little amount of water, was calculated [32]. It was found to be in the range of 101±1.76-119±1.65% (Fig. 11). Water absorption ratio was influenced by disintegrant concentration. The water absorbing power of the disintegrant increased with increase in disintegrant concentration. As observed in wetting time studies, the water absorption ratio of different disintegrants used was in the order PO>MA>LS. It is seen that there is a direct correlation between the wetting time studies, disintegration time, and water absorption ratio. The disintegrants with higher water absorbing property have less wetting time and hence minimum disintegration time.

In vitro dissolution study

The in vitro dissolution of flurbiprofen FDT’s was studied in phosphate buffer of pH 6.8 using USP XXIV dissolution test apparatus by paddle method. The release of the drug from the formulated tablets was rapid and complete with all the disintegrants used. The dissolution profiles of tablet containing PO, LS, and modified agar were in agreement with disintegration time results. It was observed that as the concentration of superdisintegrants increased from 2% to 5% w/w the release of the drug was also increased. The optimized formulation PO4 released 98.98% of drug in 4 minutes. The investigated superdisintegrants based on overall in vitro release profile can be ranked as PO > modified agar > LS. The dissolution profiles of all the FDT’s are shown in Figs. 12-15. The FDT’s PO1-PO4 released 72.40-98.98% of drug in 4 minutes study Fig. 12. Similarly, the FDT’s LS1-LS4 released 11.80-19.63% of drug in 4 minutes (Fig. 13). The FDT’s MA1-MA4 released 48.76-83.75% of drug in 4 minutes study (Fig. 14).

The FDT’s prepared with PO and Modified agar released the drug rapidly compared to tablets with LS. This is due to higher wetting and faster disintegrating property of the disintegrants PO and MA. Though the in vitro dissolution study was carried out for a total of 15-25 minutes for all formulations, 4 minutes data have been presented because the optimized tablet PO4 released almost 98.98% of drug in the same period. From the results, it could be concluded that natural superdisintegrants under study can be selected as suitable alternative to their synthetic counterparts, with added advantage of being safe and cheaper. Among the formulations, PO4 containing 8% PO was found to be optimized, as it showed good hardness, least weight variation, optimum friability, least wetting time, least disintegration time, more water absorption ratio, and maximum and complete drug release rapidly which is an ideal characteristic of a FDT (Fig. 15).

Table 2: Post-compression evaluation of flurbiprofen FDT’s prepared using PO and LS

| Parameters* | PO1* | PO2* | PO3* | PO4* | LS1* | LS2* | LS3* | LS4* |
|-------------|------|------|------|------|------|------|------|------|
| Thickness (mm) | 4.68±0.91 | 4.66±0.88 | 4.62±0.90 | 4.68±0.78 | 4.76±0.65 | 4.88±0.78 | 4.68±0.91 | 4.68±0.82 |
| Diameter (mm) | 7.10±0.79 | 7.06±0.91 | 7.08±0.98 | 7.10±0.54 | 7.00±0.65 | 7.04±0.62 | 7.10±0.64 | 7.10±0.86 |
| Hardness (kg/cm²) | 5.34±0.76 | 4.80±0.84 | 4.20±1.41 | 5.04±1.20 | 5.04±0.58 | 5.16±0.64 | 5.48±1.78 | 5.40±1.44 |
| Friability (%) | 0.07±0.45 | 0.19±0.76 | 0.19±0.65 | 0.31±0.91 | 0.34±0.98 | 0.45±1.22 | 0.28±1.66 | 0.30±0.84 |
| Weight variation (%) | 2.30±0.84 | 2.40±0.78 | 2.10±0.86 | 2.50±1.56 | 3.10±1.82 | 2.40±1.61 | 3.20±0.88 | 2.30±0.76 |
| Dispersion time (min) | 5.50±1.92 | 4.01±1.68 | 3.00±2.02 | 2.25±1.88 | 35.71±1.74 | 29.91±1.24 | 20.45±1.90 | 14.95±1.82 |
| Drug content (%) | 99.8±0.81 | 98.6±0.65 | 99.0±2.10 | 99.0±0.79 | 98.6±0.65 | 98.2±1.25 | 98.8±0.88 | 97.6±1.32 |

*Values represented as mean±SD (n=3). SD: Standard deviation, FDT’s: Fast disintegrating tablets, PO: Plantago ovate, LS: Lepidium sativum

Table 3: Post-compression evaluation of flurbiprofen FDT’s prepared using MA

| Parameters* | MA1* | MA2* | MA3* | MA4* |
|-------------|------|------|------|------|
| Thickness (mm) | 4.68±0.66 | 4.70±0.92 | 4.70±0.84 | 4.66±0.76 |
| Diameter (mm) | 7.10±0.44 | 7.10±0.26 | 7.08±0.66 | 7.10±0.78 |
| Hardness (kg/cm²) | 4.88±1.90 | 5.24±1.02 | 4.40±0.98 | 4.28±0.88 |
| Friability (%) | 0.20±0.54 | 0.18±0.68 | 0.18±0.80 | 0.25±0.74 |
| Weight variation (%) | 3.20±1.50 | 5.10±0.80 | 3.60±2.92 | 2.70±1.68 |
| Dispersion time (minutes) | 7.07±1.34 | 5.00±1.72 | 3.75±1.62 | 3.00±1.35 |
| Drug content (%) | 98.6±0.76 | 97.6±1.64 | 98.2±0.45 | 98.6±1.96 |

*Values represented as mean±SD (n=3). SD: Standard deviation, FDT’s: Fast disintegrating tablets, MA: Malt agar
Fig. 12: *In vitro* dissolution profile of fast disintegrating tablet's prepared using *Plantago ovata*. The data represent mean±standard of three determinations.

Fig. 13: *In vitro* dissolution profile of fast disintegrating tablet's prepared using *Lepidium sativum*. The data represent mean±standard of three determinations.

Fig. 14: *In vitro* dissolution profile of fast disintegrating tablet's prepared using malt agar. The data represent mean±standard of three determinations.

Fig. 15: Comparison of *in vitro* release profile of flurbiprofen fast disintegrating tablet's prepared using different superdisintegrants. The data represent mean±standard of three determinations.
Stability study
Stability studies were carried out with optimized FDT PO4 at 40±2°C/75±5% RH for the period of 6 months. The results indicated no significant changes in drug content and in vitro release (Table 4) indicating the FDT’s remained fairly stable during stability period.

CONCLUSION
Flurbiprofen FDT’s could be prepared with isolated natural superdisintegrants PO, LS and modified agar by direct compression method. All FDT’s possessed good hardness, friability, compression, disintegration, and dissolution properties. FDT’s disintegrated rapidly within the time limit. The tablets released the drug completely in short period which is advantageous for in vivo bioavailability. The natural superdisintegrants isolated showed promising results as superdisintegrants and can prove as effective alternative for synthetic disintegrants. The formulations prepared were found stable during the stability period.

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Table 4: Stability study of flurbiprofen FDT PO4

| Formulation code | Drug content* (mg) | In vitro release* (%) |
|------------------|------------------|----------------------|
|                  | Before           | After                |
| P04              | 99.0±0.13        | 98.9±0.11            |
|                  | 98.9±0.53/4 minutes | 98.22±0.74/4 minutes |

*n=3. FDT: Fast disintegrating tablet, PO4: Plantago ovata 4