

## OPTIMISATION OF IBUPROFEN FAST DISSOLVING TABLETS EMPLOYING STARCH XANTHATE USING $2^3$ FACTORIAL DESIGN

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### ABSTRACT

**Objective:** To evaluate starch xanthate as a super disintegrant in the formulation of fast dissolving tablets of poorly soluble drugs employing  $2^3$  factorial design.

**Methods:** Starch xanthate was synthesized by gelatinization process. The synthesized starch xanthate was subjected to physical and micromeritic evaluation. To establish starch xanthate as a super disintegrant, fast dissolving tablet of ibuprofen was prepared employing starch xanthate in different proportions in each case by direct compression method employing  $2^3$  factorial design. All fast dissolving tablets prepared were evaluated for drug content, hardness, friability, disintegration time and other dissolution characteristics like percent dissolved in 5 min ( $PD_5$ ), Dissolution efficiency in 5 Min ( $DE_5\%$ ) and first order rate constant ( $K_1$ ).

**Results:** The starch xanthate prepared was found to be fine, free flowing slightly crystalline powder. Starch xanthate exhibited good swelling in water. Fourier transform infrared spectra (FTIR) and Differential scanning calorimetry (DSC) study indicated the absence of interaction between ibuprofen and starch xanthate. All the fast dissolving tablets formulated employing starch xanthate were of good quality with regard to drug content ( $100\pm 5\%$ ), hardness (3.6–4 kg/sq. cm), and friability (0.12–0.15%). The disintegration time of all the formulated tablets was found to be in the range of  $13\pm 0.02$  to  $108\pm 0.02$ s. The optimized formulation FL7 has the least disintegration time i.e.,  $13\pm 0.02$ s. The *In vitro* wetting time of the formulated tablets was found to be in the range of  $90\pm 0.15$  to  $369\pm 0.17$ s. The *In-Vitro* wetting time was less (i.e., 90s) in optimized formulation FL7. The water absorption ratio of the formulated tablets was found to be in the range of  $94\pm 0.16$  to  $192\pm 0.15\%$ . The cumulative drug dissolved in the optimized formulation FL7 was found to be  $99.63\pm 0.24\%$  in 5 min.

**Conclusion:** Starch xanthate was found to be a super disintegrant which enhanced the dissolution efficiency when combined with sodium starch glycolate, croscarmellose sodium, with the ibuprofen and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 5 min.

**Keywords:** Optimization, Fast Dissolving, Superdisintegrant

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### INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50–60% of the total dosage form. Fast dissolving tablets (FDT) are solid dosage form containing indicated substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring additional water to facilitate swallowing [1]. Fast dissolving tablets offer great advantages for the patients having difficulty in swallowing [2]. The elderly constitute a major portion of today's population mainly because of the increased life span of individuals. Physiological and neurological conditions, such as dysphasia, a risk of choking, and hand tremors are leading causes of patient non-compliance in the self-administration of conventional solid oral dosage forms. Fast dissolving tablets overcome this problem and provide the advantages for paediatrics, geriatric [3], bedridden, disabled patients and also for who may have difficulty in swallowing tablets, capsules, and liquid orals. FDT will rapidly disintegrate in the mouth without the need of water [4–5]. Fast dissolving tablet formulation provides sufficient strength, quick disintegration/dissolution in the mouth without water [6], rapid dissolution and absorption of the drug, which will produce the quick onset of action. Pre gastric absorption of fast dissolving tablets can result in improved bioavailability and as a consequence of reduced dose [7]. Various techniques can be used to formulate fast dissolving tablets. Direct compression one of the techniques which require the incorporation of super disintegrant or highly water-soluble excipients into the formulation to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medication. The aim of the work was to formulate and characterize fast-dissolving tablets of ibuprofen by utilizing optimization techniques for rapid dissolution of drug and absorption employing a new super disintegrant i.e., starch xanthate.

Optimization technique provides both depth of understanding and an ability to explore and define ranges for formulation and processing factors with a rational approach to the selection of several experimental and manufacturing step for a given product, to quantitatively select a formulation. It is at this point that optimization can become a useful tool to quantitative a formulation that has been qualitatively determined.

The present investigation deals with an attempt of systematic formulation approach for optimization of ibuprofen fast dissolving tablets employing starch xanthate, sodium starch glycolate, croscarmellose sodium as super disintegrants. A  $2^3$  factorial design was applied to investigation the main and interaction effects of the three formulation variables i.e., starch xanthate (A), sodium starch glycolate (B), croscarmellose sodium (C) in each case to find the formula with less disintegration time and more dissolution efficiency 5 min and to permit arbitrary selection of tablets with immediate release of drug with in 5 min.

### MATERIALS AND METHODS

#### Materials

Sodium hydroxide, Carbon disulfide, Lactose was purchased from Finar chemicals Ltd, Ahmedabad. Potato starch, Ibuprofen, Sodium starch glycolate, Croscarmellose sodium was obtained from Yarrow chem. Products, Mumbai. Microcrystalline cellulose was bought from Qualigens fine chemicals, Mumbai. Talc and Magnesium stearate was obtained from Molychem, Mumbai.

#### Preparation of starch xanthate (a novel Superdisintegrant)

Initially, 35.4 parts of potato starch were slurried in 225 ml distilled water and 8 parts of sodium hydroxide was dissolved in

distilled water. Both are stirred continuously for 30 min. To this 5 parts of carbon disulphide was added and stirred for 16 h at 25 °C. After 16 h, it was filtered and washed with 75 ml of distilled water, 500 ml of acetone and 100 ml of ether. The product was kept in an oven at 60 °C for 2 h. The product obtained was ground and sieved.

### Characterization of starch xanthate

The starch xanthate prepared was evaluated for the following

#### Solubility

The solubility of starch xanthate was tested in water, an aqueous buffer of pH 1, 2, 3, 4, 6 and organic solvents such as alcohol, dichloromethane, chloroform, acetone and petroleum ether.

#### pH

The pH of 1% w/v slurry was measured by pH meter.

#### Melting point

Melting point was determined by using melting point apparatus.

#### Viscosity

The viscosity of 1% dispersion in water was measured using Ostwald viscometer.

#### Swelling index

Starch xanthate (200 mg) was added to 10 ml of water and light liquid paraffin taken in two Different graduated test tubes and mixed. The dispersion in the tubes was allowed to stand for 12 h. The volumes of the sediment in the tubes were recorded. The swelling index of the material was calculated as follows.

$$\text{Swelling Index \%} = \frac{\text{Volume of Sediment in water} - \text{Volume of sediment in Light Liquid Paraffin}}{\text{Volume of Sediment in Light Liquid Paraffin}} \times 100$$

#### Test for gelling property

The gelling property (gelatinization) of the starch and starch xanthate prepared was evaluated by heating a 7% w/v dispersion of each in water at 100 °C for 30 min.

#### Particle size

Particle size analysis was done by sieving using standard sieves.

#### Density

Density (g/cc) was determined by liquid displacement method using benzene as a liquid.

#### Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined by transferring the accurately weighed amount of sample in 50 ml measuring cylinder, the granules without any agglomerates and measured the volume of packing and tapped 50 times on a plane surface and tapped volume of packing recorded and LBD and TBD calculated by following formula [8].

$$LBD = \frac{\text{Mass of powder}}{\text{Volume of packing}}$$

$$TBD = \frac{\text{Mass of powder}}{\text{Tapped Volume of Packing}}$$

#### Percentage compressibility index

Percentage compressibility of powder mix was determined by Carr's Compressibility Index calculated by the following formula [9].

$$\% \text{ Carr's Index} = \frac{TBD - LBD}{TBD} \times 100$$

Where TBD= Tapped bulk density; LBD= Loose bulk density.

#### Angle of repose

The frictional forces in loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a mass of powder or granules and the horizontal plane. Angle of repose is calculated by applying the next equation;

$$\tan \theta = \frac{h}{r}, \quad \theta = \tan^{-1} \frac{h}{r}$$

Where  $\theta$ =angle of repose; h=height; r=radius

#### Fourier transform infrared (FTIR) spectroscopy

FTIR spectra of starch lactate were recorded on samples prepared in potassium bromide (KBr) disks using a BRUKER FT-IR, (Tokyo, Japan). Samples were prepared in (KBr) disks by means of a hydrostatic press at 6-8 tons pressure. The scanning range was 500 to 4000  $\text{cm}^{-1}$ .

#### X-Ray diffraction

The diffraction pattern of starch xanthate was recorded with an x-ray diffractometer (analytical spectra's Pvt. Ltd., Singapore). X-ray diffraction was performed at room temperature (30 °C) with a diffractometer; target, Cu( $\lambda$ 1.54 Å), filter, Ni; voltage, 40 kV; current 30mA; time constant 10 mm/s; scanning rate 2 °/min; measured from 2.5-50 ° at full scale 200.

#### Drug-excipients compatibility studies

The compatibility of starch xanthate with the selected drug (Ibuprofen) was evaluated in DSC and FTIR studies.

#### Differential scanning calorimetry (DSC)

DSC thermograms of ibuprofen and their mixtures (1: 1) with starch xanthate were recorded on Perkin-Elmer thermal analyzer samples (2-5 mg) were sealed into aluminum pans and scanned at a heating rate of 10 °C  $\text{min}^{-1}$  over a temperature range 30–350 °C.

#### Infrared spectroscopy

Fourier transform infra red (FTIR) spectra of ibuprofen, and their mixtures (1: 1) with starch xanthate were recorded on a Perkin-Elmer, IR Spectrophotometer model: Spectrum RXI, using KBr disc as a reference.

#### Preparation of ibuprofen fast dissolving tablets

The tablets were prepared by direct compression method employing 2<sup>3</sup> factorial design in which 3 independent variables {superdisintegrants i.e., starch xanthate (A), sodium starch glycolate (B), croscarmellose sodium (C)} and 1 dependent variable (dissolution efficiency in 5 min) were selected. The composition of the different formulation of ibuprofen fast dissolving tablets is shown in table no 1 in which the levels of super disintegrants were selected at 2 levels i.e., lower and higher level concentrations. For starch xanthate (A), the lower level i.e., 5% concentration and upper level i.e., 10% concentration. For sodium starch glycolate (B) and croscarmellose sodium (C), the lower level is 0 concentration and higher level i.e., 5% concentration. For uniformity in particle size each ingredient was passed through # 100 mesh sized screen before mixing. Starch xanthate, sodium starch glycolate, croscarmellose sodium, mannitol and microcrystalline cellulose were accurately weighed and mixed using mortar and pestle, and the added to ibuprofen. Finally, talc and magnesium stearate were added to the powder mixture. Finally, the mixed blend was compressed by using eight station rotator press Karnawathi Machineries Pvt, Ltd., Ahmedabad, India.

#### Evaluation of ibuprofen fast dissolving tablets

##### Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester and expressed in  $\text{kg/cm}^2$  [10].

##### Uniformity of weight

Weight variation test was done with 20 tablets. It is the individual variation of tablet weighed from the average weight of 20 tablets [11].

**Table 1: Formulae of ibuprofen fast dissolving tablets employing starch xanthate prepared by direct compression method involving lactose as a diluent**

Ingredients (mg/tablet)	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
Ibuprofen	100	100	100	100	100	100	100	100
Starch Xanthate	25	50	25	50	25	50	25	50
Sodium starch glycolate	---	---	25	25	---	---	25	25
Croscarmellose sodium	---	---	---	---	25	25	25	25
Lactose	155	130	130	105	130	105	105	80
Micro crystalline cellulose	200	200	200	200	200	200	200	200
Talc	10	10	10	10	10	10	10	10
Magnesium state	10	10	10	10	10	10	10	10
Total	500	500	500	500	500	500	500	500

**Table 2: Physical and micromeritics properties of the starch xanthate prepared**

Parameters*	Observation
Solubility	Insoluble in all aqueous and organic solvents tested
pH(1% w/v aqueous dispersion)	6.194
Melting point	Charred at 218 °C
Viscosity(1% w/v aqueous dispersion)	1.016 cps
Swelling index	50%
Gelling property	No gelling and the swollen particles of starch Xanthate separated from water. Where as in the case of starch, it was gelatinized and formed a gel.
Particle Size	80 µm (80/120 mesh)
Density	0.9848 g/cc
Bulk density	0.625 g/cc
Angle of repose	12.4 °
Compressibility index	32.5%

\*SD Standard Deviation from mean, n=3

### Friability

The friability of tablets was measured using a Roche friabilator. Tablets were rotated at 25 rpm for 4 min or up to 100 revolutions. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated [11].

$$F = \frac{W(\text{initial}) - W(\text{final})}{W(\text{initial})} \times 100$$

### Drug content uniformity

For content uniformity, ten tablets were weighed and powdered a quantity of powder equivalent to 10 mg of ibuprofen was extracted into 7.2 phosphate buffer and filtered. The Ibuprofen content was determined by measuring the absorbance spectrophotometrically at 254 nm after appropriate dilution with 7.2 phosphate buffer. The drug content was calculated as an average of three determinations [11].

### Wetting time

The wetting time of tablets was measured using a very simple procedure five circular tissue papers of 10 cm diameter were placed in a Petri dish with a 10 cm diameter. Ten ml of water containing a water-soluble dye (amaranth) was added to the petri dish. A tablet was carefully placed on the tissue paper. Time required for water to reach the upper surface of the tablet was noted as wetting time [12, 13].

### Water absorption ratio

A piece of tissue paper folded twice in a small petri dish containing 6 ml of water. A tablet was put in the tissue paper allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio R was determined using following equation [12, 13].

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

Where,

$W_a$  = weight of tablet after water absorption.

$W_b$  = weight of tablet before water absorption.

### In-vitro disintegration time

Disintegration time for FDTs was determined using USP disintegration apparatus 0.1 N HCl buffer. The volume of medium was 900 ml and the temperature was 37±0.2 °C. The time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured [14].

### In-vitro dissolution studies

The *in vitro* dissolution rate study of ibuprofen fast dissolving tablets were performed using 8 stage dissolution test apparatus (Electrolab TDT-08L) fitted with paddles (50 rpm) at 37±0.5 °C, using 7.2 phosphate buffer (900 ml) as a dissolution media. At the predetermined time intervals, 5 ml samples were withdrawn, filtered through a 0.45µ membrane filter, diluted and assayed at 221 nm using an Analytical technology T360 UV/Visible Double beam spectrophotometer. Cumulative percentage release was calculated using standard absorbance from the calibration curve. All the dissolution experiments were conducted in triplicate (n = 3).

### RESULTS AND DISCUSSION

The starch xanthate prepared was found to be fine, free flowing slightly crystalline powder. Therefore, starch xanthate can be used in the formulation of fast dissolving tablets. The physical and micro-meritics properties of the starch xanthate are summarized in table 2. It was insoluble in aqueous solvents and insoluble in organic solvents tested (methanol, petroleum ether, dichloromethane, and chloroform) and the pH of 0.1% aqueous dispersion was 6.196 which is suitable in the formulation of fast dissolving tablets.

Starch xanthate exhibited good swelling in water. The swelling index of starch xanthate was found to be 50%, indicating that the starch xanthate can swell and can increase the osmotic pressure inside the fast dissolving tablets upon oral administration leading to the quick disintegration of the fast dissolving tablets. All micrometric properties indicated good flow and compressibility needed for solid dosage form manufacturing. The density of starch xanthate was found to be 0.9848 g/cc.

The angle of repose and compressibility index showed good flow properties of starch xanthate. The FTIR spectrum of potato starch and starch xanthate is shown in fig. 1 and 2. The presence of peaks absorption at 1634.10 cm<sup>-1</sup> characteristic peaks of ester, so from FTIR studies it was concluded that starch xanthate (ester) was formed when starch was allowed to react with formic acid. The X-ray diffraction pattern (fig. 3) of starch xanthate showed characteristic peaks, which indicates that the structure is slightly crystalline in nature suitable for as super disintegrant in the formulation of fast dissolving tablets. The disappearance of pink color in the ester test confirmed the presence of ester, i.e., starch xanthate.

The melting point of starch xanthate was found to be 218 °C, which can resist the higher temperature during drying when used in the wet granulation method of preparation of tablets and also during accelerated stability studies. The viscosity of 1 %W/V aqueous dispersion of starch xanthate was found to be 1.016cps indicating the suitability of starch xanthate as a super disintegrant in the formulation of the fast dissolving tablets with less disintegration time. The particle size of starch xanthate was found to be 80 μ indicating the suitability of starch xanthate as a free flowing super disintegrant in the formulation of fast dissolving tablets. The starch xanthate had got all the characteristic of super disintegrants it was concluded that starch xanthate can be used as novel super disintegrant in the formulation of fast dissolving tablets.

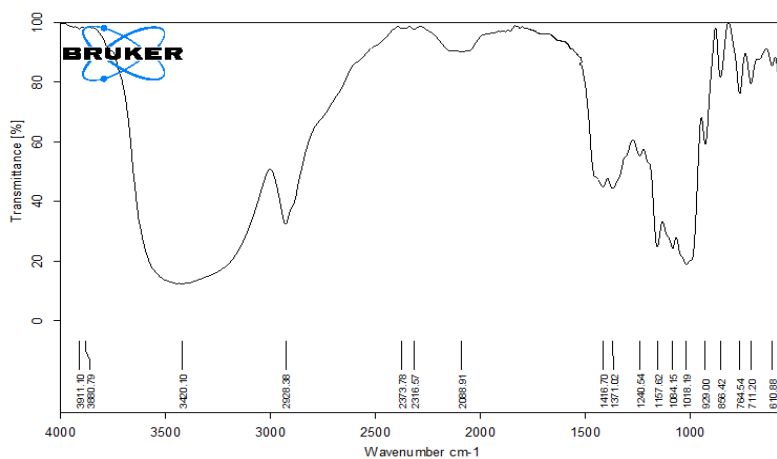
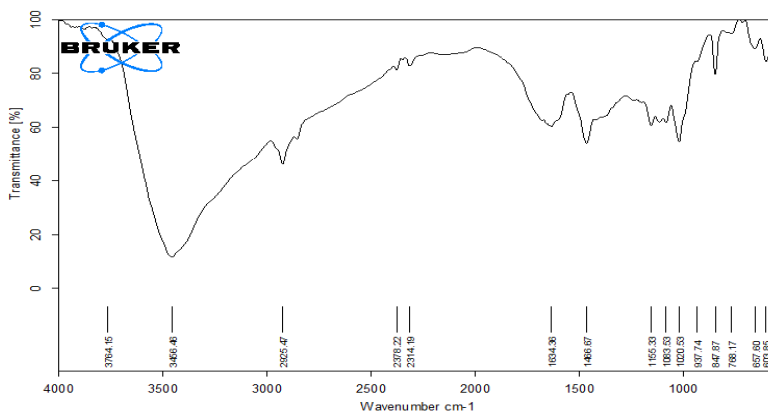


Fig. 1: Fourier transform infrared spectra of potato starch



Sample	Frequency of peak	Functional group
Starch xanthate	1634.36	(-COOH)

Fig. 2: Fourier transform infrared spectra of starch xanthate

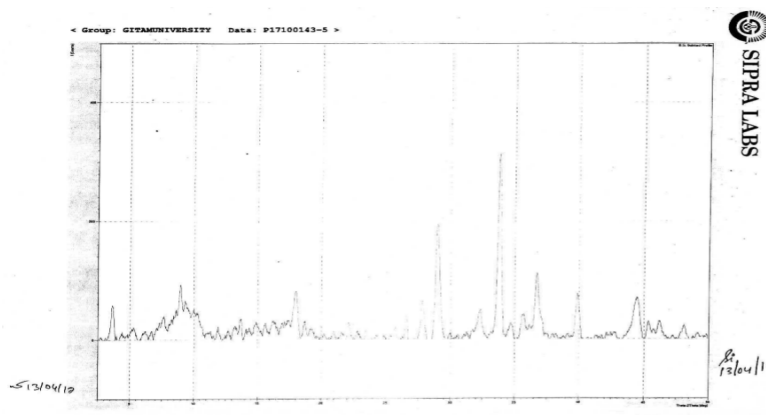


Fig. 3: X-Ray diffraction pattern of starch xanthate

The X-ray diffraction pattern of starch xanthate showed 3 characteristic peaks, which indicates that structure is slightly crystalline. The compatibility of starch xanthate with the selected drug (Ibuprofen) was evaluated by DSC and FTIR studies. The DSC thermograms of ibuprofen and ibuprofen–starch xanthate are shown in fig. 4 and 5. The DSC thermograms of ibuprofen and ibuprofen–starch xanthate exhibited exothermic peaks at 83.34 °C and 63.13 °C respectively. These melting peaks of ibuprofen and ibuprofen–starch xanthate are nearer to the melting points of ibuprofen (75-78 °C). The peaks observed in the DSC thermograms of ibuprofen and ibuprofen–starch xanthate mixtures correspond to the melting points of the respective drug indicating no interactions between the selected drug and starch xanthate polymer. The DSC

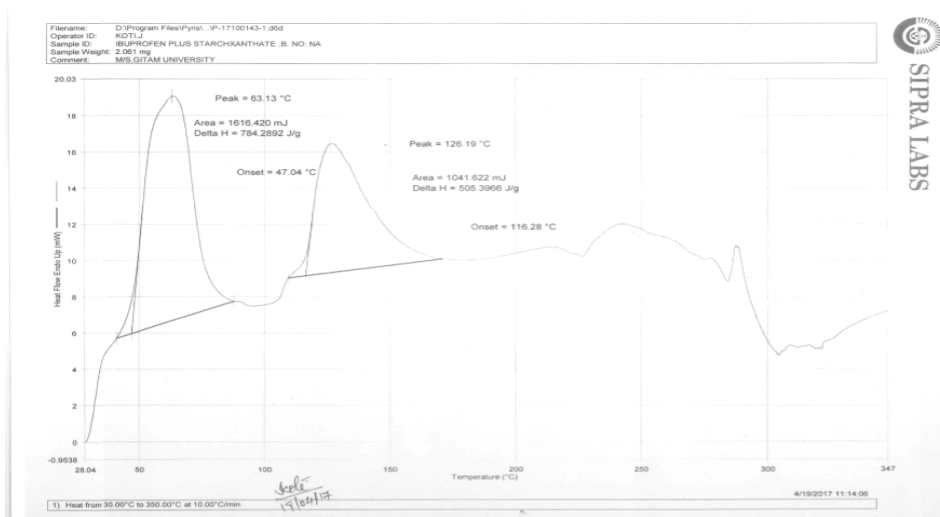
study, thus, indicated no interaction between starch xanthate and selected drug.

The FTIR spectra of ibuprofen and ibuprofen–starch xanthate are shown in fig. 6 and 7. The characteristic FTIR bands of ibuprofen at 1718.78 cm<sup>-1</sup> (COOH), and ibuprofen–starch xanthate at 1716.17 cm<sup>-1</sup>(COOH) were all observed in the FTIR spectra of both ibuprofen and ibuprofen–starch xanthate. These FTIR spectra observations also indicated no interaction between starch xanthate and the drug selected.

Thus the result of DSC and FTIR indicated no interaction between the selected drug and starch xanthate, the new super disintegrant. Hence starch xanthate could be used as a super disintegrant in the design of fast dissolving tablets of the selected drug.

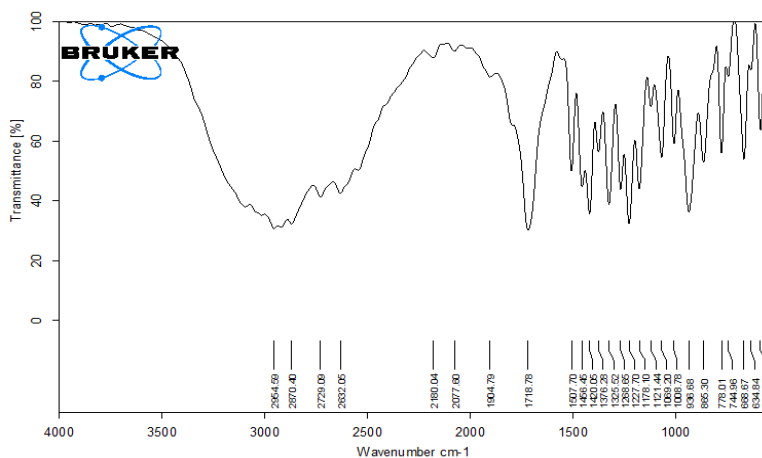
Sample	Temperature °C	
	Onset	Peak
Ibuprofen	76.31 °C	83.34 °C

Fig. 4: DSC Thermogram of ibuprofen pure drug



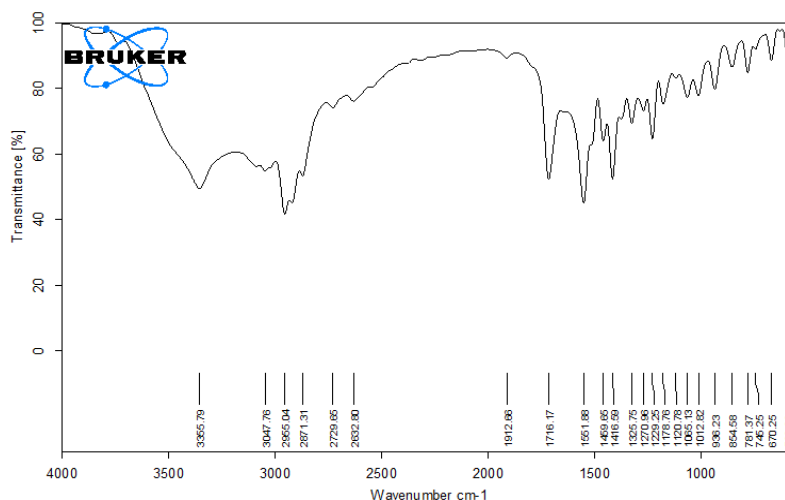
Sample	Temperature °C	
	Onset	Peak
Ibuprofen+Starch Xanthate	47.04 °C	63.13 °C

Fig. 5: DSC Thermo gram of ibuprofen with starch xanthate



Sample	Frequency of peak	Functional group
Ibuprofen	1718.78	(-COOH)

Fig. 6: FTIR spectra of ibuprofen



Sample	Frequency of peak	Functional group
Ibuprofen+Starch Xanthate	1716.17	(-COOH)

Fig. 7: FTIR spectra of ibuprofen with starch xanthate

### Evaluation of tablets

#### Hardness

Hardness of tablets from all batches was found to be in the range of  $3.6 \pm 0.03$  kg/cm<sup>2</sup> to  $4 \pm 0.01$  kg/cm<sup>2</sup>. All tablets were found hard enough so that they could easily withstand the handling and storage conditions without getting broken.

#### Friability

All the tablets exhibited acceptable friability as none of the tested batches showed percentage friability that exceeded 1%. As per IP, % friability below 1% is an indication of good mechanical resistance of the tablets. % friability of all batches found in the range of 0.12%-0.15 %. Thus, it was proved that tablets could withstand the pressure, mechanical shocks during handling, transportation, storage and manufacturing processes.

#### Drug content

Drug content of all the formulation batches was found to be between  $97.58 \pm 0.71$  to  $99.56 \pm 0.57$ . Hence, it can be concluded that all the formulations are having an accurate amount of drug distributed uniformly in powder mass and followed acceptable limits as per IP [15]. i.e. 85 to 115 % of average content table 3.

#### Disintegration studies

*In vitro* disintegration time was done by the USP dissolution apparatus. The disintegration rate has a correlation with water absorption capacity of disintegrate and The *In vitro* disintegration time was found between  $178 \pm 0.02$ - $13 \pm 0.01$ s. The outcomes were tabulated and data demonstrated in table 3. All the formulation showed disintegration time less than 180 s. It was found that the formulation FL7 will show least disintegration time 13s as compare to other formulation. The order for a disintegration time in fast dissolving tablet was found to be FL7<FL3<FL4<FL5<FL6<FL2<FL1<FL8. The order of disintegration time may be due to the interaction and main effects of the super disintegrants used in the fast dissolving tablets.

#### Water absorption ratio and wetting time

The Water absorption ratio founded between  $94 \pm 0.16$ - $192 \pm 0.15$ . This increased behaviour due to the water taking the ability of super disintegrants. The wetting time found between  $90 \pm 0.15$ - $369 \pm 0.17$ . The outcomes were tabulated and data demonstrated in table 3 and Fig. 8 and 8a. It was found that the formulation FL7 containing 5 % starch xanthate, 5 % sodium starch glycolate and 5 %

croscarmellose sodium showed less wetting time i.e.  $90 \pm 0.15$ s as compared to other formulations.

#### *In vitro* dissolution studies

Dissolution rate depends on the wetting time of the disintegrant, among all the formulations FL7 has less wetting time and has greater dissolution rate and then this is the other conformance test for correct selection of desirable. *In vitro* dissolution studies of all the formulation were done and depicted in fig. 9. In all formulations FL7 formulation was selected as the promising formulation containing 5 % starch xanthate, 5 % sodium starch glycolate and 5 % croscarmellose sodium with 99.30% release in 5 min which may be due to the interaction effect between the three super disintegrants i.e., starch xanthate, sodium starch glycolate and croscarmellose sodium at a concentration of 5 % each.

The dissolution parameters of the formulation from (FL1-FL8) which were made by direct compression method were shown in the Table: 4. In all these cases the PD<sub>5</sub> (percent dissolved in 5 min) was more (99.63) in FL7 which consists at 5 % starch xanthate, 5 % sodium starch glycolate and 5 % croscarmellose sodium. The same was in the case of DE<sub>5</sub> % (dissolution efficiency in 5 min). The PD<sub>5</sub> and DE<sub>5</sub> % reveals that starch xanthate was effective at 5% starch xanthate, 5% sodium starch glycolate, and 5 % croscarmellose sodium when the formulations were made by direct compression using these super disintegrants. The order for a PD<sub>5</sub> in fast dissolving tablet was found to be FL1<FL2<FL4<FL8<FL6<FL5<FL3<FL7. The K<sub>1</sub> also increased in all the formulation when compared to the F1 formulation. The number of folds increases in DE<sub>5</sub>% and the number of folds increase in K<sub>1</sub> (min<sup>-1</sup>) was given in table 4. The order for a DE<sub>5</sub>% in fast dissolving tablet was found to be FL8<FL1<FL2<FL4<FL6<FL5<FL3<FL7. The order of PD<sub>5</sub> and DE<sub>5</sub>% may be due to the interaction and main effects of the super disintegrants used in the fast dissolving tablets. From the results, it was concluded that starch xanthate (new super disintegrant) could be used as a super disintegrant in the formulation of fast dissolving tablets of ibuprofen.

To evaluate the individual and combined effects of the three factors involved, fast dissolving tablets were formulated employing selected combinations of the factors as per 2<sup>3</sup>-factorial design. The fast dissolving tablets and release parameters (percent drug released in 5 min) of the fast dissolving formulated were analyzed as per ANOVA of 2<sup>3</sup>-factorial design. ANOVA of fast disintegrating times (table 5) indicated that the individual effects of starch xanthate (A), sodium starch glycolate (B) and croscarmellose sodium (C), as well as the combined effects of AB, AC, BC and ABC factors, were



significant ( $P < 0.05$ ) on disintegration time and dissolution efficiency in 5 min of ibuprofen fast dissolving tablets.

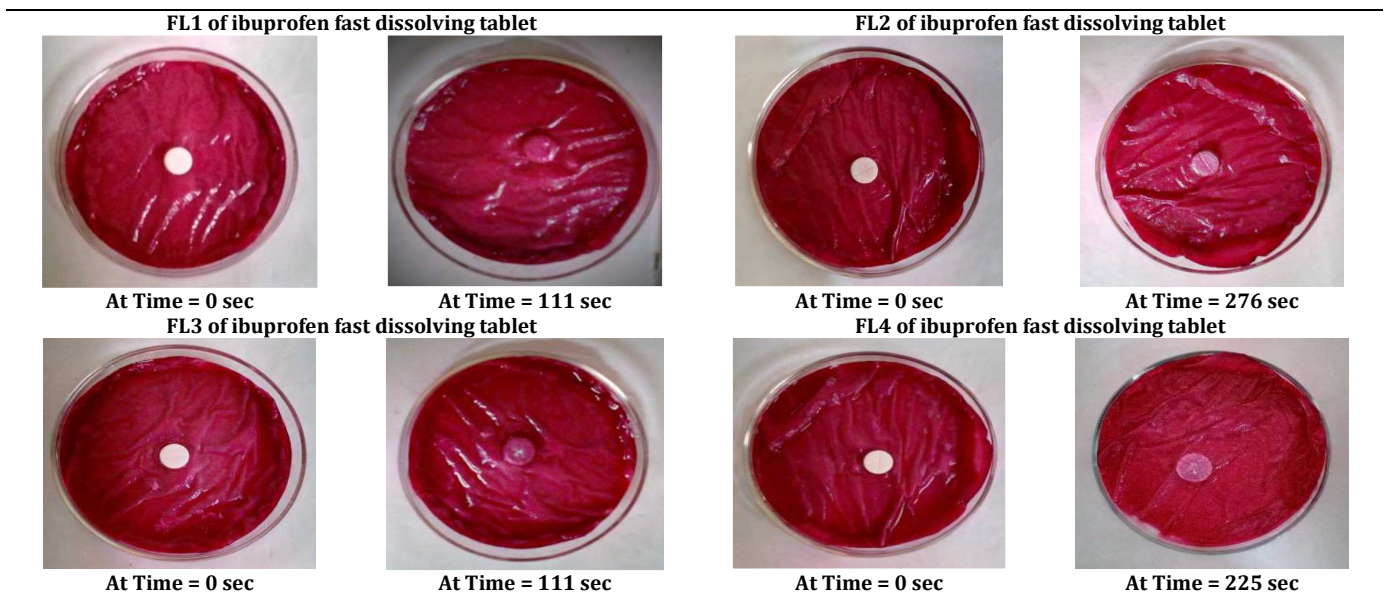
Fast dissolving tablets formulated employing starch xanthate (5%), sodium starch glycolate (5%) and croscarmellose sodium (5%) as super disintegrants exhibited in disintegration and dissolution

efficiency in 5 min. Formulation FL7 gave release of 99.63% in 5 min fulfilling the official specification, based on disintegration time and dissolution efficiency in 5 min. Formulation FL7 is considered as a good fast dissolving tablet formulations of ibuprofen which was found to better than the ibuprofen fast dissolving tablets formulated by Sai Kishore *et al* [16].

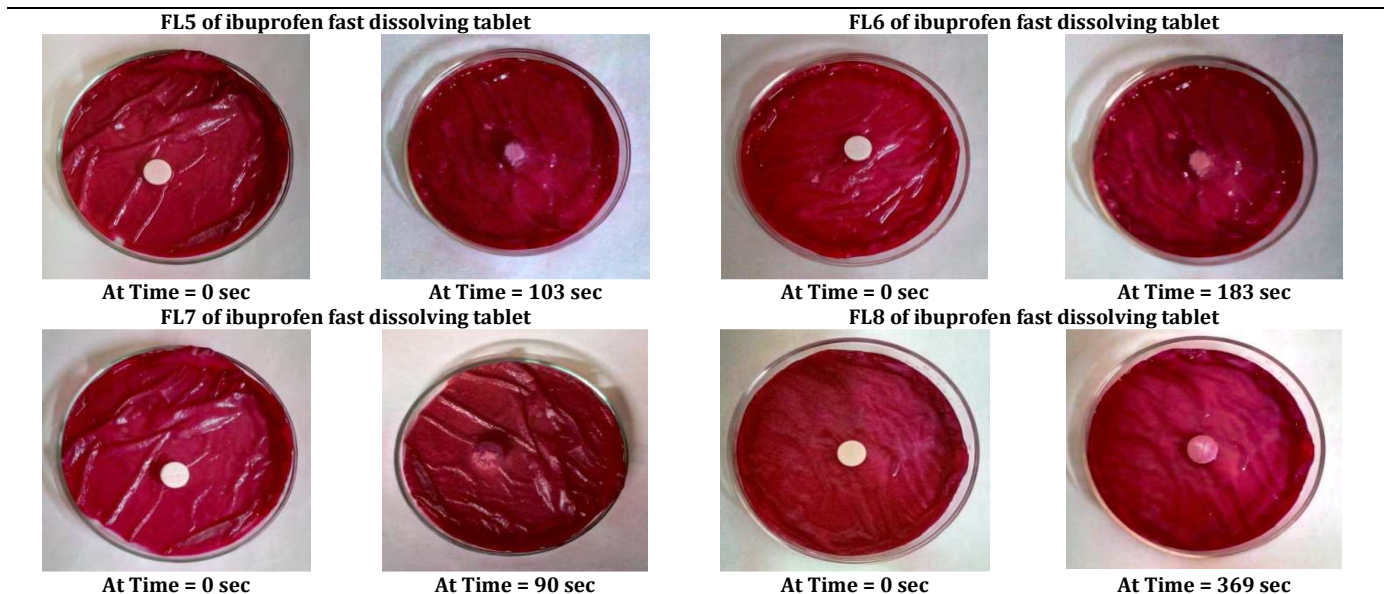
**Table 3: Physical properties: hardness, friability drug content of ibuprofen fast dissolving tablets prepared by direct compression method involving lactose as a diluent**

Formulation	Hardness (kg/cm <sup>2</sup> )n±SD	Friability (%)n±SD	Drug Content mg/tab) n±SD	Disintegration Time (sec) n±SD	Wetting Time (s) n±SD	Water Absorption Ratio (%) n±SD
FL1	3.9±0.01	0.12±0.013	97.58±0.71	108±0.02	310±0.02	145±0.12
FL2	3.6±0.03	0.13±0.015	98.10±0.79	103±0.03	276±0.12	137±0.18
FL3	4.0±0.01	0.14±0.012	99.45±0.63	14±0.02	111±0.09	94±0.16
FL4	3.8±0.04	0.12±0.014	98.56±0.55	25±0.02	225±0.02	134±0.15
FL5	3.7±0.03	0.14±0.012	99.23±0.56	83±0.01	103±0.21	139±0.21
FL6	3.9±0.01	0.15±0.012	99.34±0.18	95±0.02	183±0.09	111±0.12
FL7	3.7±0.02	0.14±0.014	99.56±0.57	13±0.01	90±0.15	192±0.15
FL8	4.0±0.04	0.12±0.013	99.17±0.11	178±0.02	369±0.17	126±0.27

\*SD Standard Deviation from mean, n=3



**Fig. 8: Ibuprofen fast dissolving tablets prepared employing starch xanthate involving lactose as a diluent**



**Fig. 8a: Ibuprofen fast dissolving tablets prepared employing starch xanthate involving lactose as a diluents**

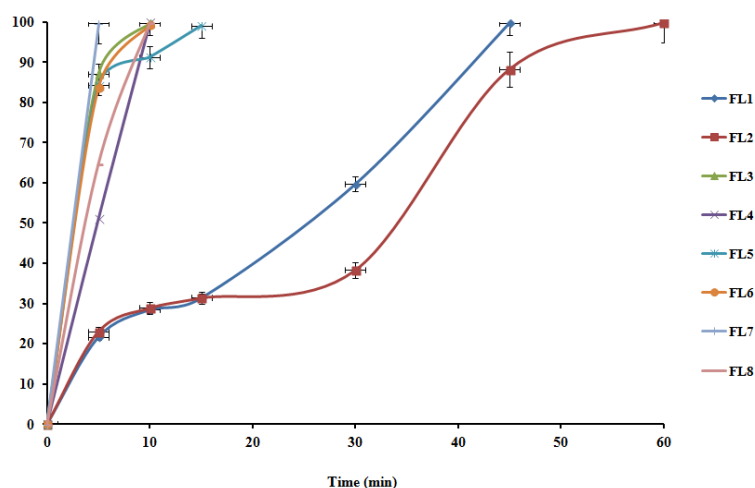


Fig. 9: Dissolution profiles of ibuprofen fast dissolving tablets prepared employing starch xanthate involving lactose as a diluents, (FL1-FL8) (n=6, mean±SD)

Table 4: Dissolution parameters of ibuprofen fast dissolving tablets formulated employing starch xanthate and other known super disintegrants prepared by direct compression method involving lactose as a diluent

Dissolution parameters*	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8
PD <sub>5</sub>	21.65	22.97	87.13	51.08	84.33	83.78	99.63	64.82
DE <sub>5</sub> %	4.7	8.2	41.3	22.4	40.6	38.9	48.3	2.7
No of folds increase in DE <sub>5</sub> %	-	1.74	8.78	4.76	8.63	8.27	10.27	4.82
K <sub>1</sub> (min <sup>-1</sup> )	0.01	0.04	0.39	0.25	0.26	0.41	-	0.21
No of folds increase in K <sub>1</sub> (min <sup>-1</sup> )	-	4	39	25	26	41	-	21

\*SD Standard Deviation from mean, n=3, PD<sub>5</sub>-Percent dissolved in 5 min., DE<sub>5</sub>%-Dissolution efficiency in 5 min., K<sub>1</sub>=First Order Rate Constant

Table 5: ANOVA of dissolution efficiency in 5 min of ibuprofen fast dissolving tablets formulated employing starch xanthate involving lactose as a diluent

Source of variation	d. f	S. S	M. S. S	Variance ratio	Result
Replicates	2	0.81	0.40	0.50	P > 0.05
Treatments	7	5563.31	794.75	1006.01	P < 0.05
Starch xanthate (5%)	1	25421.55	25421.55	32179.17	P < 0.05
Strach xanthate (10%)	1	33.37	33.37	42.24	P < 0.05
Starch xanthate (5%) X Sodium starch glycolate (5%)	1	2137.59	2137.59	2705.81	P < 0.05
Starch xanthate(10%) X Sodium starch glycolate (5%)	1	62.72	62.72	79.39	P < 0.05
Starch xanthate(5%) X Croscarmellose sodium (5%)	1	4306.76	4306.76	5451.59	P < 0.05
Starch xanthate(10%) X Croscarmellose sodium (5%)	1	171.20	171.20	216.70	P < 0.05
Starch xanthate(5%) X Sodium starch glycolate(5%) X Croscarmellose sodium (5%)	1	250.26	250.26	316.78	P < 0.05
Starch xanthate(10%) X Sodium starch glycolate(5%) Croscarmellose sodium X (5%)	1	385.60	385.60	488.10	P < 0.05
Error	14	11.12	0.79	--	--
Total	23	--	--	--	--

\*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; p>0.05 indicate non-significance, d. f-Degree of Freedom \*S. S-Sum of Square \*M. S. S-Mean Sum of Squares, ANOVA= Analysis of Variance

## CONCLUSION

Starch xanthate is an efficient super disintegrant for fast dissolving tablets. The disintegration and dissolution efficiency of the fast dissolving tablets of Ibuprofen was good and depended on the concentration of super disintegrant employed i.e., starch xanthate, sodium starch glycolate, croscarmellose sodium. The formulated fast dissolving tablets of Ibuprofen exhibited good dissolution efficiency in 5 min which can be used for the fast therapeutic action of ibuprofen.

Overall, Starch xanthate was found to be a super-disintegrant which enhanced the dissolution efficiency when combined with sodium starch glycolate and croscarmellose sodium, with the ibuprofen and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 5 min.

## ABBREVIATION

FTIR-Fourier transform infrared spectra, DSC-Differential scanning calorimetry, ANOVA-Analysis of variance, PD<sub>5</sub>-Percent dissolved in 5 min, DE<sub>5</sub>%-Dissolution efficiency in 5 min

## CONFLICT OF INTERESTS

Declare none

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