



International Journal of ChemTech Research

CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555

Vol.10 No.7, pp 32-48, 2017

Design, Optimisation and Evaluation of Aceclofenac Fast Dissolving Tablets Employing Starch Xanthate-A New Superdisintegrant

R.Santosh Kumar*, V.Goutham Kumar and T.Naga Satya Yagnesh

Gitam Institute of Pharmacy, Gitam University, Rushikonda, Visakhapatnam, A.P 530045, India

Abstract : The purpose of the present study is to evaluate starch xanthate as a superdisintegrant in the formulation of fast dissolving tablets of poorly soluble drugs. Starch xanthate was synthesized by gelatinization process. The synthesized starch xanthate was subjected to physical and micromeritic evaluation. To establish starch xanthate as a superdisintegrant, fast dissolving tablet of aceclofenac 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 PD_5 , DE_5 and K_1 . The starch xanthate prepared was found to be fine, free flowing slightly crystalline powder. Starch xanthate exhibited good swelling in water. The swelling index was 50% all micrometric properties indicated good flow and compressibility needed for solid dosage from manufacturing. All the fast dissolving tablets formulated employing starch xanthate were of good quality with regard to drug content, hardness and friability and fulfilled the official (IP/USP) requirements of compressed tablets with regard to the above mentioned physical properties. Starch xanthate was found to be a superdisintegrant which enhanced the dissolution efficiency when combined with sodium starch glycolate, crosscarmellose sodium, with the aceclofenac and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 5 minutes.

Key Words : Fast dissolving, Superdisintegrant, Starch xanthate, Dissolution efficiency.

Introduction:

The concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional means of taking their medication¹. Fast dissolving tablets are solid dosage form containing indicated substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring additional water to facilitate swallowing. Fast dissolving tablets offer great advantages for the patients having difficulty in swallowing. It has been reported that dysphasia (difficulty in swallowing) is usual among all groups and more specific with pediatric, geriatric population along with patients have nausea, retching, and motion sickness complications [1]. Fast dissolving tablets overcome this problem and provide the advantages for pediatrics, geriatric [2-3], 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 FDT 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 superdisintegrant 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 aceclofenac by utilizing optimization techniques for rapid dissolution of drug and absorption employing a new superdisintegrant i.e., starch xanthate.

Optimization Technique:

Optimization technique provide both a 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 aceclofenac fast dissolving tablets employing starch xanthate, sodium starch glycolate, crosscarmellose sodium as superdisintegrants. A 2³ 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), crosscarmellose 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 disulphide, mannitol was purchased from Finar chemicals Ltd, Ahmedabad. Potato starch, Aceclofenac, sodium starch glycolate, crosscarmellose 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 35.4g of potato starch was slurried in 225ml distilled water and 8g of sodium hydroxide was dissolved in distilled water. Both are stirred continuously for 30minutes. To this 5ml of carbon disulphide was added and stirred for 16hours at 25⁰C.After 16 hours it was filtered and washed with 75ml of distilled water, 500ml of acetone and 100ml of ether. The product was kept in oven at 60⁰C for 2 hrs. The product obtained was ground and sieved.

Characterization of starch xanthate:

The starch xanthate prepared was evaluated for the following

Solubility:

Solubility of starch xanthate was tested in water, aqueous buffer of pH 1,2,3,4, and 6.196 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:

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.

$S.I (\%) = \frac{\text{Volume of sediment in water} - \text{volume of sediment in light liquid paraffin}}{\text{Volume of sediment in light liquid paraffin}} \times 100$

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 optical microscopy method.

Density:

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

Bulk density[8]:

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined by transferring the accurate 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.

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

$TBD = \frac{\text{Mass of powder}}{\text{Tapped volume of packing}}$

Percentage compressibility index [9]

Percentage compressibility of powder mix was determined by Carr's compressibility index calculated by the following formula.

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

$\tan \theta = h/r$; $\theta = \tan^{-1} (h/r)$, where θ =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 cm^{-1} .

X – Ray diffraction:

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(λ 1.54 Å), filter, Ni; voltage, 40 kV; current 30mA; time constant 10mm/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 (aceclofenac) was evaluated FTIR studies.

Infrared spectroscopy:

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

Preparation of aceclofenac fast dissolving tablets:

The tablets were prepared by direct compression method employing 2³ factorial design in which 3 independent variables {superdisintegrants i.e., starch xanthate (A), sodium starch glycolate (B), crosscarmellose sodium (C)} and 1 dependent variable (dissolution efficiency in 5 min) were selected. The composition of different formulation of aceclofenac fast dissolving tablets is shown in Table no 1 in which the levels of superdisintegrants 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 crosscarmellose sodium (C), the lower level is zero 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, crosscarmellose sodium, mannitol and microcrystalline cellulose were accurately weighed and mixed using mortar and pestle, and the added to aceclofenac. Finally talc and magnesium stearate were added to the powder mixture. Finally mixed blend was compressed by using eight station rotator press Karnawathi Machinerics Pvt, Ltd., Ahmedabad, India).

Evaluation of aceclofenac fast dissolving tablets:**Hardness test[10]**

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 kg/cm²

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.

Friability:

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

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

Drug content uniformity [11]:

For content uniformity, ten tablets were weighed and powdered a quantity of powder equivalent to 10mg of aceclofenac was extracted into 7.4 phosphate buffer and filtered. the aceclofenac content was determined by measuring the absorbance spectrophotometrically at 274 nm after appropriate dilution with 7.4 phosphate buffer. The drug content was calculated as an average of three determinations.

Wetting time[12,13]:

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.

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 ration R was determined using following equation.

$$R = 100 (W_a - W_b) / W_b$$

Where,

W_a = weight of tablet after water absorption.

W_b = weight of tablet before water absorption.

***In – vitro* disintegration time[14]:**

Disintegration time for FDTs was determined using USP disintegration apparatus 0.1 N HCl buffer. The volume of medium was 900 ml and temperature was $37 \pm 0.2^{\circ}\text{C}$. The time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.

***In – vitro* dissolution studies⁵:**

The *in- vitro* dissolution rate study of aceclofenac fast dissolving tablets were performed using 8 stage dissolution test apparatus (Electrolab TDT-08L) fitted with paddles (50 rpm) at $37 \pm 0.5^{\circ}\text{C}$, using 7.4 phosphate buffer (900 ml) as a dissolution media. At the predetermined time intervals, 5 ml samples were withdrawn, filtered through 0.45μ membrane filter, diluted and assayed at 274 nm using a 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. The physical and micromeritics 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) the pH of 0.1% aqueous dispersion was 6.196.

Starch xanthate exhibited good swelling in water. The swelling index was 50% all micrometric properties indicated good flow and compressibility needed for solid dosage from 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^{-1} characteristic peak 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. The disappearance of pink color in the ester test confirmed the presence of ester, i.e., starch xanthate. As the starch xanthate was slightly crystalline powder and it had got all the characteristic of superdisintegrants it was concluded that starch xanthate can be used as novel superdisintegrant in the formulation of fast dissolving tablets.

The compatibility of starch xanthate with the selected drug (aceclofenac) was evaluated by FTIR studies. The FTIR spectra of aceclofenac and aceclofenac – starch xanthate are shown in Figs.4 and 5. The characteristic FTIR bands of aceclofenac at 3617.25 cm^{-1} (COOH), and aceclofenac – starch xanthate at 3317.01 cm^{-1} (cooh) were all observed in the FTIR spectra of both aceclofenac and aceclofenac – starch xanthate. These FTIR spectra observations also indicated no interaction between starch xanthate and the drug selected.

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

Fast dissolving tablets each containing 100 mg of aceclofenac could be prepared by employing starch xanthate and other known superdisintegrants, sodium starch glycolate and crosscarmellose sodium by direct compression method. Hardness of the tablet was in the range of 3.6 – 4 kg/sq.cm. it indicates good strength with a capability to resist physical and pre functionary stress conditions during handling. Weight loss on the friability test was less than 0.15 % in all cases.

All the fast dissolving tablets prepared contained aceclofenac within $100 \pm 5\%$ of the labelled claim. As such the prepared tablets were of good quality with regard to drug content, hardness and friability. The disintegration time of all the formulated tablets was found to be in the range of 10 ± 0.02 to 51 ± 0.02 seconds as indicated in the Table: 3.

The result of *In-Vitro* wetting time and water absorption ratio was found to be within the prescribed limits and satisfy the criteria of the dissolving tablets (Fig: 6, 6a & 6b). The *In – Vitro* wetting time was less in F6 which consists of combination of 10 % starch xanthate, and 5 % crosscarmellose sodium.

The drug dissolution from the aceclofenac fast dissolving tablets employing starch xanthate and other known superdisintegrants were in the Table: 4. and Fig: 7 and 8. The dissolution parameters of the formulation from (F1–F9) which were made by direct compression method were shown in the Table: 6.4. In all these cases the PD₅ (percent dissolved in 5 minute) was more in F6 which consists at 10 % starch xanthate, and 5 % crosscarmellose sodium. The same was in the case of DE₅ % (dissolution efficiency in 5 min). The PD₅ & DE₅ % reveals that starch xanthate was effective at 10% and 5 % crosscarmellose sodium when the formulations were made by direct compression using these superdisintegrants. The k_1 decreased in all the formulation when compared to F9 formulation. which was given in the Table 5. From the results it was concluded that starch xanthate (new superdisintegrant) could be used as superdisintegrant in the formulation of fast dissolving tablets of aceclofenac.

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 2³-factorial design. The fast dissolving tablets and release parameters (percent drug released in 5mins) of the fast dissolving formulated were analyzed as per ANOVA of 2³-factorial design. ANOVA of fast disintegrating times (Table 6) indicated that the individual effects of starch xanthate (A), sodium starch glycolate (B) and crosscarmellose sodium (C) as well as the combined effects of AB, AC, BC and ABC factors were significant on disintegration time and dissolution efficiency in 5 min of aceclofenac fast dissolving tablets.

ANOVA of dissolution efficiency in 5 min (Table 6) indicated that the individual effects as well as combined effects of the three factors (i.e., starch xanthate, sodium starch glycolate and crosscarmellose sodium) were all significant ($p < 0.05$). The ANOVA results thus indicated that the three factors have significantly influence on the disintegration time and dissolution efficiency in 5 min.

Fast dissolving tablets formulated employing starch xanthate (10%), and crosscarmellose sodium (5%) as superdisintegrants exhibited in disintegration and dissolution efficiency in 5 min. Formulation 6 gave release of 100% in 15mins fulfilling the official specification, based on disintegration time and dissolution efficiency in 5 min. Formulation 6 is considered as a good fast dissolving tablet formulations of aceclofenac.

Table: 1: Formulae of aceclofenac fast dissolving tablets employing starch xanthate prepared by direct compression method involving mannitol as diluent.

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|-----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Aceclofenac | 100 | 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 | --- |
| Crosscarmellose sodium | --- | --- | --- | --- | 25 | 25 | 25 | 25 | --- |
| Mannitol | 155 | 130 | 130 | 105 | 130 | 105 | 105 | 80 | 180 |
| Micro crystalline cellulose | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| Talc | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Magnesium stearate | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Total | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |

Table: 2. Physical and micromeritic 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 ⁰ 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 gel. |
| Particle Size | 80 μ m (100 mesh) |
| Density | 0.9848 g/cc |
| Bulk Density | 0.625 g/cc |
| Angle of Repose | 12.4 ⁰ |
| Compressibility Index | 32.5% |

Table.3: Physical properties: hardness, friability drug content of aceclofenac fast dissolving tablets prepared by direct compression method involving mannitol as diluent.

| Formulation | Hardness (kg/cm ²)n± S.D | Friability (%)n± S.D | Drug Content mg/tab) n± S.D | Disintegration Time (sec) n± S.D | Wetting Time (sec) n± S.D | Water Absorption Ratio (%) n± S.D |
|-------------|--------------------------------------|----------------------|-----------------------------|----------------------------------|---------------------------|-----------------------------------|
| F1 | 3.9 ± 0.01 | 0.12 ± 0.013 | 97.58 ± 0.71 | 16 ± 0.02 | 14 ± 0.02 | 39± 0.12 |
| F2 | 3.6 ± 0.03 | 0.13 ± 0.015 | 98.10 ± 0.79 | 13 ± 0.03 | 22± 0.12 | 40± 0.18 |
| F3 | 4.0 ± 0.01 | 0.14 ± 0.012 | 99.45 ± 0.63 | 14±0. 02 | 33 ± 0.09 | 112 ± 0.16 |
| F4 | 3.8 ± 0.04 | 0.12 ± 0.014 | 98.56 ± 0.55 | 51 ±0. 02 | 150 ± 0.02 | 108 ± 0.15 |
| F5 | 3.7 ± 0.03 | 0.14 ± 0.012 | 99.23 ± 0.56 | 20 ± 0.01 | 90 ± 0.21 | 69 ± 0.21 |
| F6 | 3.9 ± 0.01 | 0.15 ± 0.012 | 99.34 ± 0.18 | 10 ± 0.02 | 05± 0.09 | 131 ± 0.12 |
| F7 | 3.7 ± 0.02 | 0.14 ± 0.014 | 99.56 ± 0.57 | 15 ±0. 01 | 51± 0.15 | 131 ± 0.15 |
| F8 | 4.0 ± 0.04 | 0.12 ± 0.013 | 99.17 ± 0.11 | 38± 0.02 | 193 ± 0.17 | 122± 0.27 |
| F9 | 3.6 ± 0.03 | 0.12 ± 0.013 | 97.34 ± 0.71 | 50 ± 0.02 | 148 ± 0.17 | 29 ± 0.12 |

Table 4: Aceclofenac percent dissolved from dissolving tablets employing starch xanthate prepared by direct compression method involving mannitol as diluent.

| Time (mins) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| 5 | 2.51 ±0.13 | 24.24 ±0.23 | 66.56 ±0.18 | 2.83 ±0.44 | 1.39 ±0.28 | 96.75 ±0.32 | 3.63±0.34 | 6.33±0.13 | 44.22 ±0.38 |
| 10 | 86.62 ±0.46 | 37.06 ±0.48 | 75.98 ±0.22 | 56.06 ±0.18 | 58.33 ±0.41 | 99.89 ±0.41 | 5.87 ±0.14 | 45.65 ±0.16 | 88.72 ±0.46 |
| 15 | 99.89 ±0.17 | 49.62 ±0.17 | 79.04 ±0.16 | 66.53 ±0.24 | 98.17 ±0.47 | 100.70±0.14 | 15.39 ±0.27 | 48.84 ±0.26 | 99.64 ±0.35 |
| 30 | --- | 56.42 ±0.38 | 87.02 ±0.49 | 96.66 ±0.34 | --- | --- | 17.81 ±0.34 | 51.47 ±0.38 | --- |
| 45 | --- | 99.56 ±0.21 | 99.89 ±0.37 | --- | --- | --- | 19.31 ±0.24 | 80.16 ±0.44 | --- |
| 60 | --- | --- | --- | --- | --- | --- | 22.95 ±0.42 | 99.13 ±0.34 | --- |

Table 5: Dissolution parameters of aceclofenac fast dissolving tablets formulated employing starch xanthate and other known superdisintegrants prepared by direct compression involving mannitol as diluent

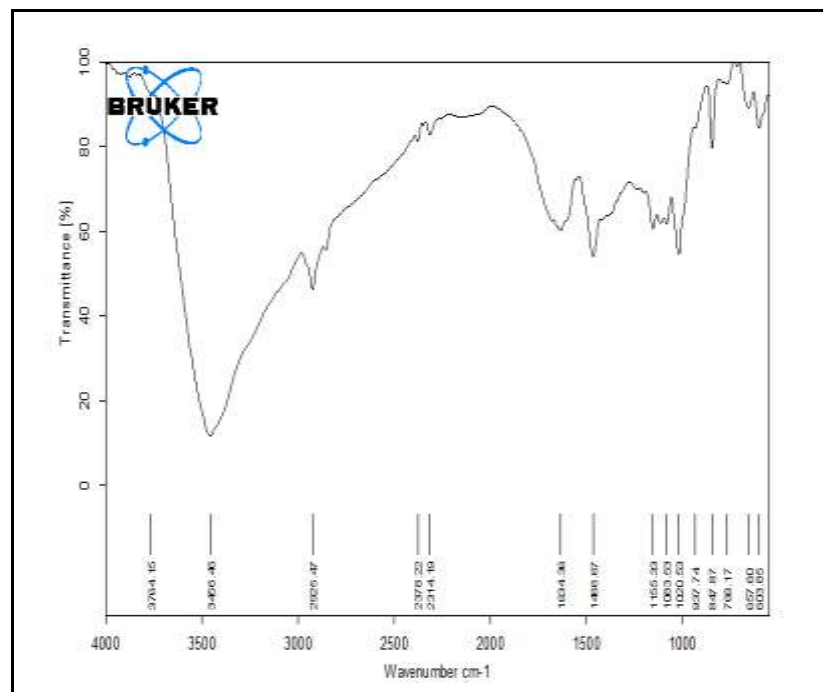
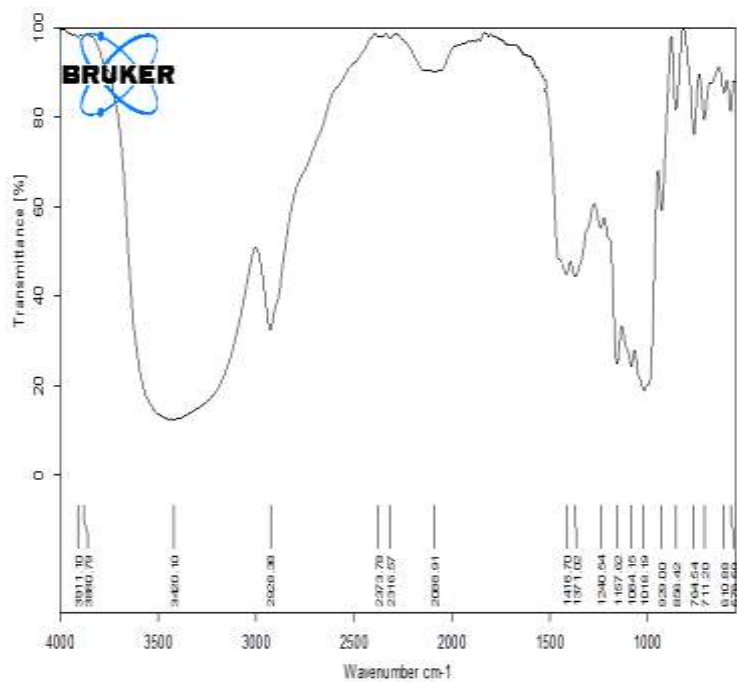
| Time(mins) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|------|-------|-------|------|------|-------|------|------|-------|
| PD ₅ | 2.51 | 24.24 | 66.56 | 2.83 | 1.39 | 96.75 | 3.63 | 6.33 | 44.22 |
| DE ₅ % | 7.2 | 8.5 | 31.1 | 15.2 | 3.8 | 43.7 | 0.8 | 5.0 | 8.6 |
| No of folds increase in DE ₅ % | 0.83 | 0.98 | 3.61 | 1.76 | 0.44 | 5.08 | 0.09 | 0.58 | --- |
| K ₁ (min ⁻¹) | 0.22 | 0.04 | 0.06 | 0.06 | 0.09 | 0.01 | 0.01 | 0.02 | 0.23 |
| | | | | | | | | | |

Table 6 ANOVA of dissolution efficiency in 5 min of aceclofenac fast dissolving tablets formulated employing starch xanthate involving mannitol as diluent

| Source of Variation | d. f | S.S | M.S.S | Variance ratio | Result |
|--|------|---------|---------|----------------|----------|
| Replicates | 2 | 0.33 | 0.165 | 0.12 | P > 0.05 |
| Treatments | 7 | 4758.43 | 679.77 | 531.07 | P < 0.05 |
| Starch xanthate (5%) | 1 | 4975.52 | 4975.52 | 3887.12 | P < 0.05 |
| Strach xanthate (10%) | 1 | 317.55 | 317.55 | 248.08 | P < 0.05 |
| Starch xanthate (5%) X Sodium starch glycolate (5%) | 1 | 1931.42 | 1931.42 | 1508.91 | P < 0.05 |
| Starch xanthate(10%) X Sodium starch glycolate (5%) | | 163.80 | 163.80 | 127.96 | P < 0.05 |
| Starch xanthate(5%) X Crosscarmellose sodium (5%) | 1 | 28.82 | 28.82 | 22.51 | P < 0.05 |
| Starch xanthate(10%) X Crosscarmellose sodium (5%) | 1 | 1274.58 | 1274.58 | 995.76 | P < 0.05 |
| Starch xanthate(5%) X Sodium starch glycolate(5%) X Crosscarmellose sodium (5%) | 1 | 1931.42 | 1931.42 | 1508.92 | P < 0.05 |
| Starch xanthate(10%) X Sodium starch glycolate(5%) Crosscarmellose sodium X (5%) | 1 | 941.25 | 941.25 | 735.35 | P < 0.05 |
| Error | 14 | 18.01 | 1.28 | -- | -- |
| Total | 23 | -- | -- | -- | -- |

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



| Sample | Frequency of Peak | Functional Group |
|-----------------|-------------------|------------------|
| Starch Xanthate | 1634.36 | (-COOH) |

Fig: 1. Fourier transform infrared spectra of potato starch

Fig: 2. Fourier transform infrared spectra of starch xanthate

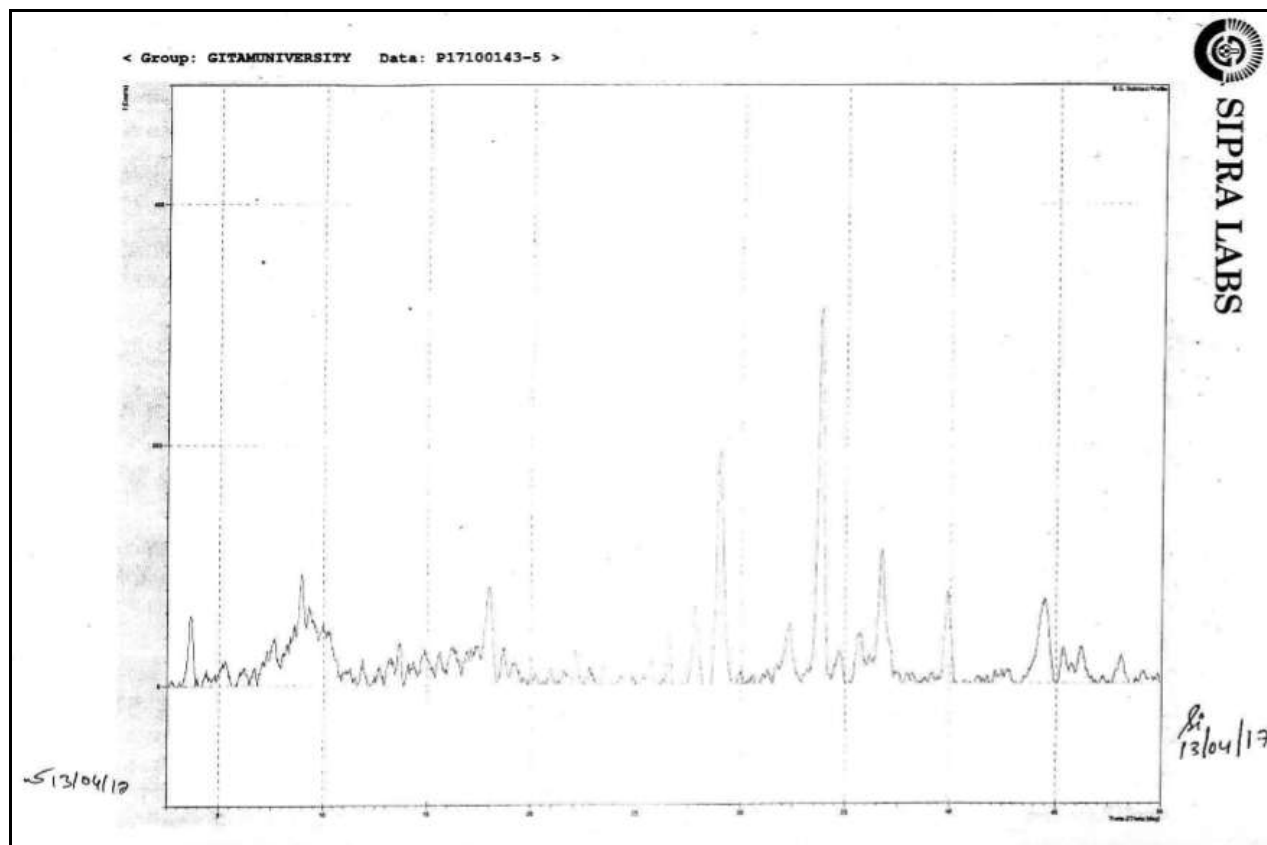
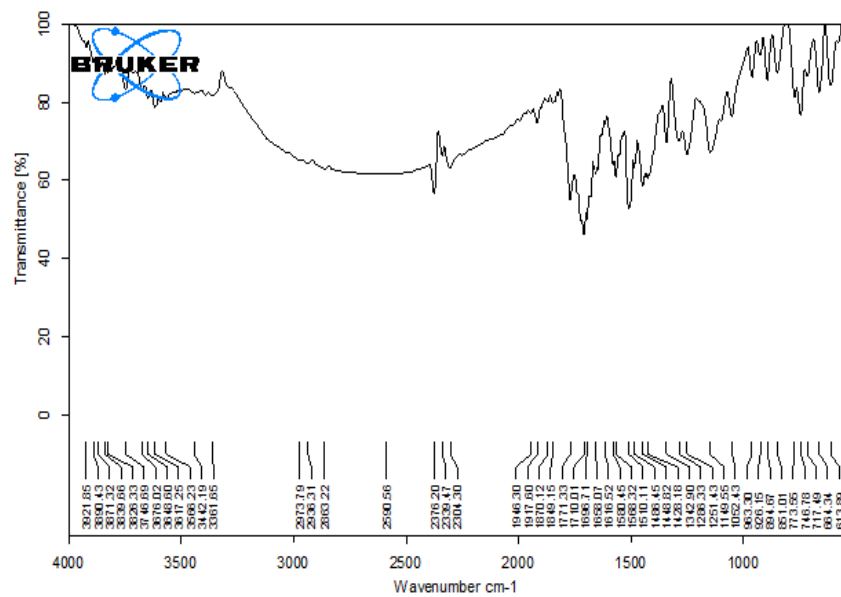


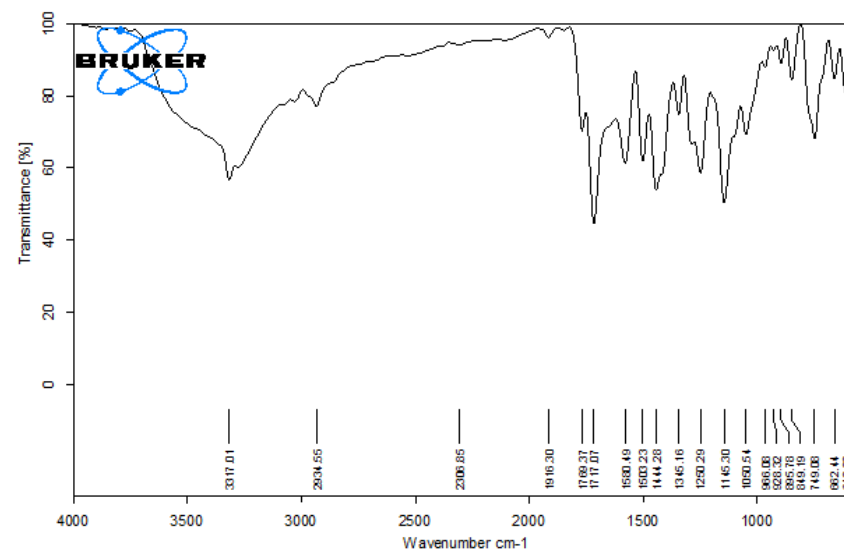
Fig: 3.X-Ray diffraction pattern of starch xanthate

The X-ray diffraction pattern of starch xanthate showed 3 characteristics peaks, which indicates that structure is slightly crystalline.



| Sample | Frequency of peak | Functional group |
|-------------|-------------------|------------------|
| Aceclofenac | 3617.25 | (-COOH) |

Fig .4. FTIR spectra of aceclofenac



| Sample | Frequency of peak | Functional group |
|-------------------------------|-------------------|------------------|
| Aceclofenac + Starch Xanthate | 3317.01 | (-COOH) |

Fig .5. FTIR Spectra of aceclofenac with starch xanthate

Fig 6: Aceclofenac fast dissolving tablets prepared employing starch xanthate involving mannitol as diluent

F1 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 14 sec

F2 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 22 sec

F3 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 33 sec

F4 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 150 sec

Fig 6a: Aceclofenac fast dissolving tablets prepared employing starch xanthate involving mannitol as diluent

F5 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 90 sec

F6 of Aceclofenac Fast Dissolving Table



At Time = 0 sec



At Time = 05 sec

F7 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 51 sec

F8 of Aceclofenac Fast Dissolving Tablet



At Time = 0 sec



At Time = 193 sec

Fig 6b: Aceclofenac fast dissolving tablets prepared employing starch xanthate involving mannitol as diluent

F9 of Aceclofenac Fast Dissolving Tablet



At Time=0 sec



At time=148 sec

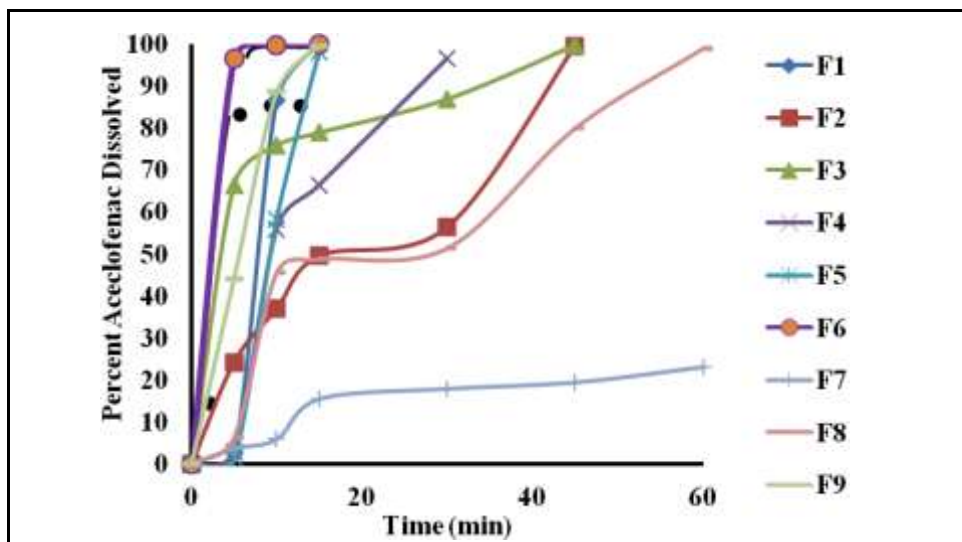


Fig 7: Dissolution profiles of aceclofenac fast dissolving tablets prepared employing starch xanthate involving mannitol as diluent (F1-F9)

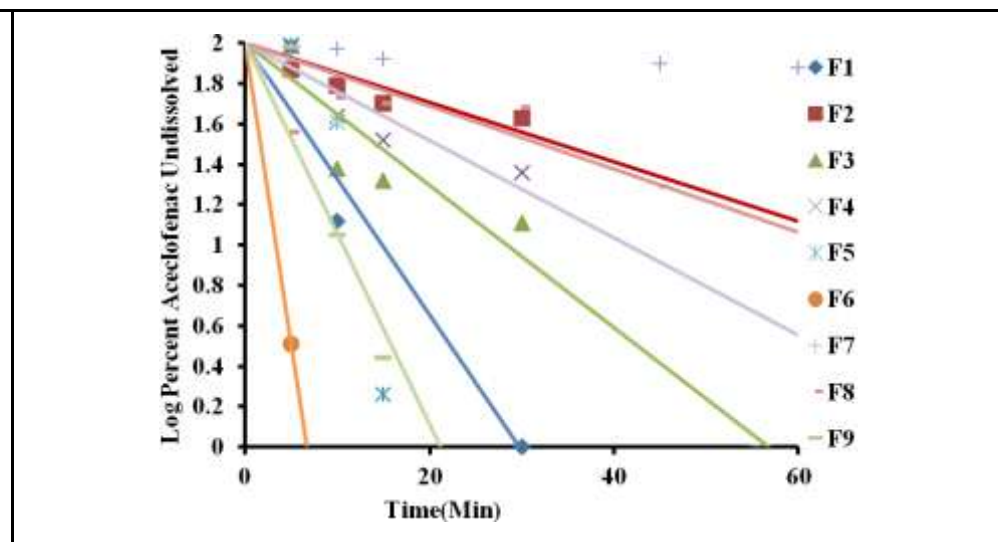


Fig 8: Time Vs Log percent drug undissolved plots for aceclofenac fast dissolving tablets prepared employing starch xanthate involving mannitol as diluent (F1- F9)

Conclusion:

Starch xanthate is an efficient superdisintegrant for fast dissolving tablets. The disintegration and dissolution efficiency of the fast dissolving tablets of aceclofenac was good and depended on the concentration of superdisintegrant employed i.e., starch xanthate(10%), and crosscarmellose sodium (5%). The formulated fast dissolving tablets of aceclofenac employing starch xanthate and crosscarmellose sodium exhibited good dissolution efficiency in 5 min which can be used for the fast therapeutic action of aceclofenac. Overall, Starch xanthate was found to be a superdisintegrant which enhanced the dissolution efficiency when combined with crosscarmellose sodium, with the aceclofenac and hence it could be used in the formulation of fast dissolving tablets to provide immediate release of the contained drug within 15minutes.

Abbreviations:

FTIR - Fourier transform infrared spectra
DSC - Differential scanning calorimetry
ANOVA – Analysis of variance
PD₅-Percent dissolved in 5 minutes
DE₅%- Dissolution efficiency in 5 minutes

References

1. Bradoo R, Shahani S, Poojary S, Fast dissolving drug delivery systems; JAMA, 2001, 4, 27-31.
2. Seager H, Drug delivery product and zydis-fast dissolving dosage form; J Pharm Pharmacol, 1998,50, 375-82.
3. Abdelbary G, Prinderre P, Couani C, Taochim J, Reynier JP, Riccerelle P; The preparation of orally disintegrating tablets using a hydrophilic waxy binder, Int J Pharm; 2004, 278, 2, 423-33.
4. Sastry SV, Nyshadham JR, Fix JA; Recent technological advances in oral drug delivery: a review, Pharm Sci Technol Today; 2000, 3,4,138-45.
5. Lachman L, Libermann HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd edition; 1991. p. 233-5.
6. Biradar S, Bhagavati S, Kuppasad I; Fast dissolving drug delivery system: A brief overview, Internet J Pharmacol; 2005, 4:2. edition; 1991. p. 233-5.
7. Indurwade NH, Rajyaguru TH, Nakhat PD; Novel approach-fast dissolving tablets, Indian Drug 2002; 38, 8, 405-9.
8. The United States Pharmacopoeia 29, National Formulary 24, Asian Edition. Rockville, MD: United States Pharmacopoeia Convention, Inc; 2006. p. 1890.
9. Jacob S, Shirwaikar A, Joseph A, Srinivasan KK; Novel co-processed excipient of mannitol and microcrystalline callous for preparing fast dissolving tablet of Glipizide, Indian J Pharm Sci; 2007, 69, 5, 633-9.
10. Hiremath JG, Shastry CS, Srinath MS; Pharmaceutical approaches of taste masking in oral dosage forms, Indian Drugs; 2004, 41, 253-7.
11. Abdelbary A, Elshafeey AH, Zidan G; Comparative effects of different cellulosic-based directly compressed orodispersible tablets on oral bioavailability of famotidine, Carbohydrate Polymers; 2009,77, 799-806.
12. Battu SK, Michael AR, Soumyajit M, Madhusudan Y; Formulation and evaluation of rapidly disintegrating fenoverine tablets: effect of super disintegrants, Drug Dev Ind Pharm; 2007, 33, 1225-32.
13. Goel H, Vora N, Rana V; A novel approach to optimize and formulate fast disintegrating tablets for nausea and vomiting, AAPS PharmSciTech; 2008, 9, 774–8.
14. Puttewar TY, Kshirsagar MD, Chandewar AV, Chikhale RV; Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin, J King Saud University (Sci); 2010, 22, 229–40.

Extra page not to be printed.

For your Research References requirements, please log on to=

www.sphinxesai.com

International Journal of ChemTech Research
