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# Development and Characterization of Fast Disintegrating Tablets of Piroxcam

**Kiran Thadkala[1]*,Ramchander Thadkapally[1], Rajkumar Devara[1], Durgaprasad Kemisetti[1]**

[1,*]**Mother Teresa College of Pharmacy, Hyderabad, AP, India.**

***Corres. author: kiran.thadkala@gmail.com.***

**Abstract:** Objective: The study was aimed to formulate fast disintegrating of piroxicam by using superdisintegrants. Development of oral fast disintegrating drug delivery is to give fast relief and also to overcome difficulty in swallowing tablets that leads to non-compliance and ineffective therapy. Piroxicam fast disintegrating tablets were prepared by using direct compression method and were characterized for both pre-compression and post-compression physical parameters. From the in-vitro drug release studies the optimized formulation showed fast drug release (above 99%) within the 15 minutes when compared with conventional tablet prepared in a similar manner with normal disintegrating agent. Differential scanning calorimetry (DSC) study was carried out to understand the drug-polymer compatibility and revealed that there was no possible interaction between them. Thus usage of superdisintegrants to develope fast disintegrating tablets may be suitable to give rapid drug delivery and rapid onset of action.

**Keywords**: Fast disintegrating drug delivery, Superdisintegrants, Pre-compression, Post-compression, Differential scanning calorimetry, Drug-polymer compatibility.

## INTRODUCTION

Oral administration of different dosage forms is the most commonly used method due to greater flexibility in design of dosage form and high patient acceptance, but many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. To overcome above problems formulating the Fast disintegrating drug delivery is one approach [1-4]. They are useful in patients, such as pediatric, geriatric, and bedridden or mentally disabled who may face difficulty in swallowing conventional tablets or capsules and liquid orals or syrups leading to ineffective therapy [5]. Fast disintegrating drug delivery can be achieved by various conventional methods like direct compression, wet granulation, molding, spray drying, freeze drying, and sublimation [6-7]. The oral fast disintegrating tablet is also known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar. According to Pharmacopoeia, the oral fast disintegrating tablet should disperse/disintegrate in less than three minutes [8].

Direct compression method is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in this method. Fewer unit operations and excipients compared with wet granulation (shorter processing time and lower energy consumption) and fewer stability issues for drugs that are sensitive to heat or moisture are the advantages of direct compression method [9-10]. The key properties of oral fast disintegrating tablets are fast absorption of water into the core of the tablets, and disintegration of associated particles into individual components for fast disintegration [11]. The presence of superdisintegrant lowers the disintegration time without much affecting the tablet properties. The concentration of lubricant is critical factor since it prevents wetting and there by increases the disintegration time of the fast disintegrating tablets [12].

The basic approach in development of fast disintegrating drug delivery is use of superdisintegrant, which plays an important role in the disintegration and dissolution of tablet. The selection of a suitable disintegrant and its optimum concentration are able to ensure quick disintegration and high dissolution rates. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of super disintegrant, the wetted surface of the carrier increases that promote the wettability and dispersibility of the system, leads to enhance the disintegration and dissolution. Superdisintegrants are selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant. Common superdisintegrants used in this formulation are sodium starch glycolate, crospovidone and croscarmellose sodium [13-14].

Piroxicam is a member of the phenylalkanoic acid derivative family of non-steroidal anti-inflammatory drugs. Non-steroidal anti-inflammatory drugs are widely used for the long-term treatment of chronic rheumatic diseases such as rheumatoid arthritis and osteoarthritis [15]. Piroxicam is classified as poorly water soluble drug and it is primarily intended to treat painful conditions, which requires fast release of drug [16]. By considering these factors, it is required to prepare a Piroxicam fast disintegrating tablets to facilitate fast release of drug there by rapid onset of action.

## MATERIALS AND METHODS

### MATERIALS

Piroxicam was gift sample from gift sample from Vilin Biomed Ltd, Rurki, India. Sodium Starch Glycolate, Crosspovidone, Crosscarmelose and Avicel PH 102 were gift samples from Matrix laboratories, Hyderabad, India. All other chemicals used were of analytical grade.

### PREPARATION OF FAST DISINTEGRATING TABLETS

Fast disintegrating tablets (FDT's) were prepared by direct compression method. Piroxicam, Superdisintegrants (Sodium Starch Glycolate, Crosspovidone, and Crosscarmelose) other tabletting excipients were passed through a mesh no 60. The drug was mixed with proper portion of superdisintegrant. Care should be taken to confirm the proper mixing of drug and superdisintegrant. Then excipients other than glidant and lubricant were added and mixed in a poly bag for 5-10 minutes. The obtained blend was lubricated with talc and magnesium stearate for another 5 minutes and the resultant mixture was directly compressed into tablets with 6 mm round flat punches using 16 station rotary tabletting machine (Cadmach, Ahmedabad, India). The compositions of the fast disintegrating tablets are given in Table 1. The conventional Piroxicam tablets (control) were prepared in a similar manner without using superdisintegrants.

### PRE-COMPRESSION PARAMETERS

The powder mixtures of different formulations were evaluated for angle of repose, bulk density (apparent and tapped) and compressibility index. The fixed funnel method was employed to measure the angle of repose (θ) and it was calculated using the following formula:

$$\text{Tan } \theta = h/r \qquad [1]$$

In which, θ is angle of repose, h is height of the cone and r is radius of the cone base. Angle of repose less than $30^0$ shows the free flowing of the material. The tapping method was used to determine the tapped density, bulk density and percent compressibility index. The compressibility index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities and is calculated using the following formulas:

$$\text{Carr's Index} = [(\rho_{tap} - \rho_b) / \rho_{tap}] / \times 100 \qquad [2]$$

In which, $\rho_b$ is bulk density and $\rho_{tap}$ is tapped density.

### POST-COMPRESSION PARAMETERS

The prepared tablets were studied for their physical properties like weight variation, hardness, friability, drug content uniformity, in-vitro disintegration time, in-vitro dispersion time, wetting time, water absorption ratio and mouth feel. For estimating weight variation, 20 tablets of each formulation were weighed using an Electronic weighing balance (AW 120, Shimadzu Corporation, Japan). The strength of tablet is expressed by measuring hardness ($Kg/cm^2$) friability. The hardness of six tablets was measured using Monsanto tablet hardness tester. Friability was determined on ten tablets in a Roche friabilator (Electrolab, Mumbai, India) for 4 min at 25 rpm.

### DETERMINATION OF DRUG CONTENT

For estimation of drug content, ten tablets were finely powdered; quantities of the powder equivalent to 50 mg of piroxicam were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml of methanol and allowed to stand for 5 h with intermittent sonication to ensure complete solubility of the drug. The mixture was made up to volume with methanol. The solution was suitably diluted and the absorption was by UV-Visible spectrophotometer (Systronics 2202, Ahmedabad, India) at 333nm. The drug concentration was calculated from the calibration curve.

**IN VITRO DISINTEGRATION TIME**

In vitro disintegration time of FDT's was determined by following the procedure described by Gohel et al. Briefly, 10 ml of water at room temperature was taken in a petri dish of 10 cm in diameter. The tablet was then carefully placed in the centre of petri dish and the time required for the tablet to completely disintegrate into fine particles was noted. Measurements were carried out in triplicates [17-18].

**IN VITRO DISPERSION TIME**

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6ml of pH 6.8 (simulated saliva fluid). Three tablets from each formulation were randomly selected & in vitro dispersion time is expressed in seconds [19].

**WETTING TIME**

Wetting time was determined as described in the literature elsewhere. Briefly, two circular tissue papers were placed in a Petri dish of 10 cm diameter. Ten milliliter of water containing 0.5 (% w/v) of phenol red was added to the petri dish. The dye solution was used to identify the complete wetting of the tablet surface. A tablet was care fully placed on the surface of the paper in the petri dish at room temperature. The time required for water to reach the upper surface of tablet and to completely wet them was noted as wetting time. Wetting time was recorded using stop watch and the measurements were carried out in triplicates [20].

**WATER ABSORPTION RATIO**

The weight of the tablet prior to placement in the petri dish was noted ($W_b$) using digital balance (Shimadzu, Japan). The wetted tablet was removed and reweighed ($W_a$). Water absorption ratio (R), was then calculated according to the following equation,[21]

$$R = \frac{W_a - W_b}{W_b} \times 100 \qquad [3]$$

$W_b$ and $W_a$ were tablet weights before and after water absorption, respectively.

**IN-VITRO DISSOLUTION STUDY**

The release of piroxicam from FDT's was carried out using USP XXIV Type II (paddle method) dissolution apparatus (Electro lab, TDT-08L) at a rotation speed of 100 rpm, and a temperature of 37±0.5 °C. The drug release studies were carried out in 1.2 pH buffer. An aliquot of 5 ml was collected at predetermined time intervals (2, 5, 10, 15 and 30 minutes) and replaced with fresh dissolution medium. The samples were filtered, by passing through 0.45 µm membrane filters (Millipore, USA) and analyzed spectrophotometrically at 333 nm.

Cumulative percent drug release was plotted as a function of time and percent drug release in 15 minutes ($Q_{15}$) was calculated. Initial dissolution rate (IDR) was calculated as percentage dissolved of drug over the first 15 minutes per minute. Dissolution efficiency (DE) was calculated from the area under the dissolution curve at time t (measured using the trapezoidal rule) and expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time [22]. Relative dissolution rate (RDR) is the ratio between amount of drug dissolved from optimized formulation and that dissolved from the conventional formulation at 15 minutes [23].

**DRUG- POLYMER INTERACTION STUDY**

To study the possible interaction between piroxicam and excipients, DSC study was carried out on pure piroxicam, Sodium starch glycolate, croscarmellose sodium, crospovidone and optimized formulation (F6). Differential thermal analysis thermograms were obtained using DSC (Perkin-Elmer, Shelton, U.S). The analyses were performed under nitrogen (nitrogen flow rate 50 ml/min) in order to eliminate oxidative and pyrrolytic effects at a standard heating rate of 15ºC/minute over a temperature range of 50ºC - 350ºC.

**Table 1: Formulation of Piroxicam fast disintegrating tablets prepared by direct compression method**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Piroxicam | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Sodium Starch Glycolate | 4 | 6 | 8 | - | - | - | - | - | - |
| Crospovidone | - | - | - | 4 | 6 | 8 | - | - | - |
| Croscarmelose | - | - | - | - | - | - | 4 | 6 | 8 |
| Avicel pH 102 | 32 | 30 | 28 | 32 | 30 | 28 | 32 | 30 | 28 |
| Mannitol | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| Sodium Lauryl Sulphate | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 |
| Aspartame | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 | 1.6 |
| Talc | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 |
| Magnesium Stearate | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 | 0.8 |

All the ingredient weights are given in mg per one tablet. Each tablet weight is 80 mg.

**Table 2: Characterization of powder mixture**

| Formulation | Angle of Repose* | Bulk density | Tapped density | % Carr's Index |
|---|---|---|---|---|
| F1 | 29.12±1.24 | 0.321 | 0.402 | 20.149 |
| F2 | 27.11±1.14 | 0.323 | 0.403 | 19.743 |
| F3 | 29.56±1.86 | 0.315 | 0.402 | 21.641 |
| F4 | 30.65±1.35 | 0.332 | 0.412 | 19.417 |
| F5 | 29.13±1.26 | 0.302 | 0.378 | 20.105 |
| F6 | 29.56±1.46 | 0.323 | 0.398 | 18.844 |
| F7 | 25.12±1.13 | 0.291 | 0.354 | 17.796 |
| F8 | 26.12±1.13 | 0.311 | 0.362 | 14.088 |
| F9 | 27.12±1.13 | 0.325 | 0.405 | 19.753 |

* All values represent mean ± standard deviation, n=6

**Table 3: Physical properties of Piroxicam fast disintegrating tablets**

| Formulation | Weight variation* (mg) | Hardness† ($Kg/cm^2$) | Friability (%) | Drug content Uniformity‡ (%) |
|---|---|---|---|---|
| F1 | 80.15 ± 1.83 | 3.4±0.46 | 0.34 | 96.2±0.38 |
| F2 | 79.12 ± 1.44 | 3.2±0.62 | 0.38 | 98.9±0.25 |
| F3 | 81.8 ± 1.12 | 3.0±0.44 | 0.14 | 99.5±0.46 |
| F4 | 80.3 ± 0.14 | 3.2±0.22 | 0.26 | 97.2±0.74 |
| F5 | 80.45 ± 0.33 | 3.5±0.84 | 0.35 | 99.8±0.34 |
| F6 | 78.23± 1.15 | 3.2±0.51 | 0.38 | 98.2±1.72 |
| F7 | 82.14 ± 0.74 | 3.4±0.34 | 0.27 | 96.8±0.61 |
| F8 | 80.72 ± 0.28 | 3.0±0.28 | 0.22 | 97.4±0.26 |
| F9 | 81.12 ± 1.26 | 3.2±0.65 | 0.16 | 96.3±1.74 |

* All values represent mean ± standard deviation, n=20
† All values represent mean ± standard deviation, n=6
‡ All values represent mean ± standard deviation, n=3

**Table 4: Physical properties of Piroxicam fast disintegrating tablets**

| Formulation | In-vitro Disintegration Time* (sec) | In-vitro Dispersion Time* (sec) | Wetting Time* (sec) | Water Absorption Ratio* | $Q_{15}$* | Mouth Feel |
|---|---|---|---|---|---|---|
| F1 | 58.36 ± 0.12 | 74.26±1.28 | 42.14±1.15 | 37.14± 1.12 | 63.9 ± 0.58 | Acceptable |
| F2 | 48.28 ± 0.48 | 75.43±1.45 | 41.38±1.24 | 31.32± 1.26 | 74.43 ± 0.12 | Acceptable |
| F3 | 46.23 ± 0.28 | 67.64±1.26 | 34.63±1.46 | 36.27± 1.48 | 91.24 ± 0.26 | Acceptable |
| F4 | 53.38 ± 0.16 | 84.32±1.46 | 31.84±1.12 | 36.26± 1.34 | 86.23 ± 0.42 | Acceptable |
| F5 | 49.36 ± 0.45 | 70.22±1.68 | 38.64±1.18 | 30.22± 1.16 | 88.96 ± 0.35 | Acceptable |
| F6 | 32.68 ± 0.53 | 61.28±1.36 | 30.28±1.44 | 39.46± 1.36 | 99.43 ± 0.29 | Acceptable |
| F7 | 44.55 ± 0.42 | 72.64±1.42 | 34.45±1.32 | 38.24± 1.35 | 86.73 ± 0.13 | Acceptable |
| F8 | 40.15 ± 0.36 | 91.28±1.24 | 44.28±1.68 | 32.13± 1.22 | 89.35 ± 0.47 | Acceptable |
| F9 | 33.42 ± 0.29 | 61.32±1.26 | 30.12±1.14 | 39.24± 1.42 | 99.24 ± 0.25 | Acceptable |

* All values represent mean ± standard deviation, n=3

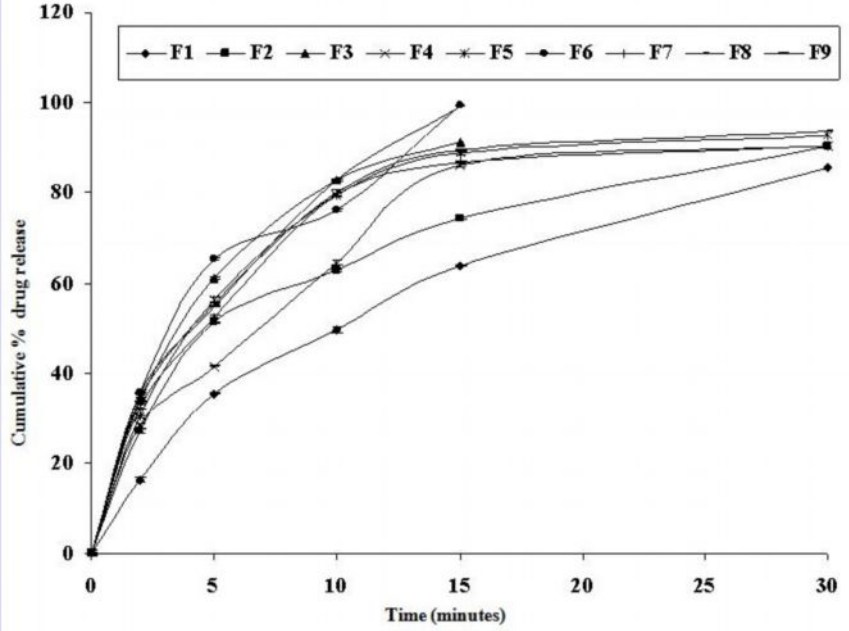
**Table 5: Dissolution Parameters of optimized and control Piroxicam formulations**

| Formulation | $Q_{15}$* | IDR (%/min) | DE | RDR |
|---|---|---|---|---|
| **Optimized (F6)** | 99.43±0.29 | 6.63 | 65.32 | 1.718±0.08 |
| **Optimized (F9)** | 99.24±0.25 | 6.62 | 64.61 | 1.715±0.08 |
| **Conventional** | 57.98±0.34 | 3.86 | 18.90 | |

$Q_{15}$-percent drug release in 15 minutes, IDR-initial dissolution rate, DE-dissolution efficiency and RDR- relative dissolution rate.

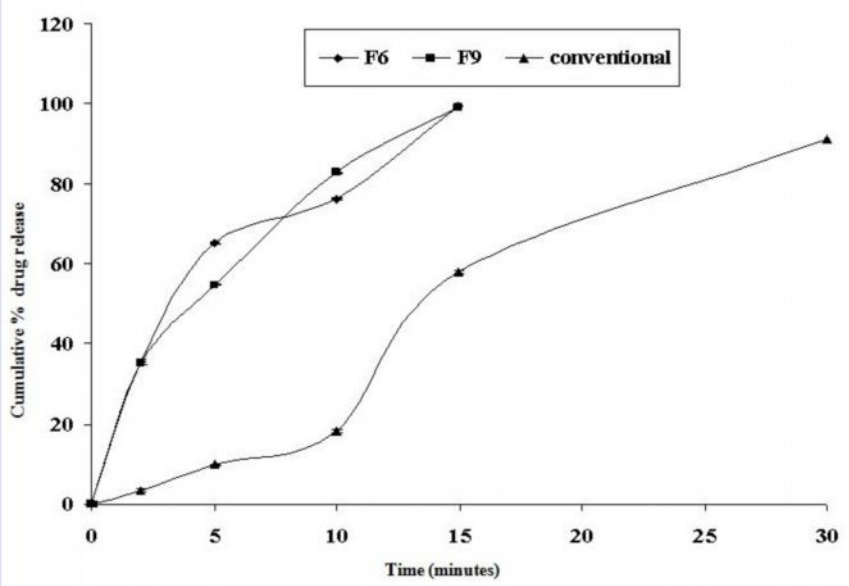
* All values represent mean ± standard deviation, n=3

**Figure 1: Release profile of Piroxicam from FDT's prepared by using different percentages of Superdisintegrants**



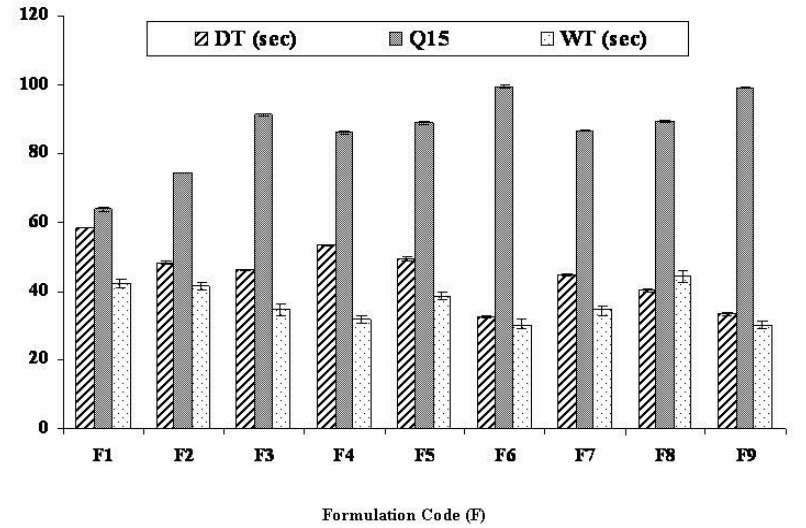

All values are expressed as mean ± SD (n=3)

**Figure 2: Comparison of drug release profile of Optimized formulations (F6, F9) and Conventional tablet of Piroxicam**



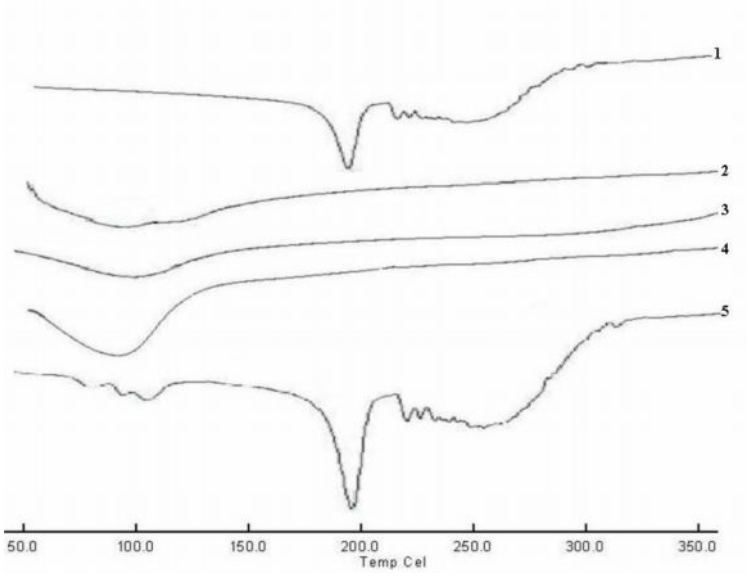

All values are expressed as mean ± SD (n=3)

**Figure 3: Comparison of response variables: Disintegration time (DT in sec), %Drug release in 15 min (Q15) and Wetting time (WT in sec)**




All values are expressed as mean ± SD (n=3)

**Figure 4: DSC thermograms of 1) Piroxicam 2) Sodium starch glycolate 3) Croscarmellose 4) Crospovidone 5) Optimized formulation (F6)**




## RESULTS AND DISCUSSION

### PRE-COMPRESSION PARAMETERS

The powder mixtures of different formulations were evaluated for angle of repose, bulk density (apparent and tapped), compressibility index and their values were shown in Table 2.The apparent bulk density and tapped bulk density values ranged from 0.291 to 0.332 and 0.354 to 0.412 respectively. The results of angle of repose and compressibility index (%) ranged from 25.12±1.13 to 30.65±1.35 and 14.088 to 21.641 respectively. The results of angle of repose (<30) and compressibility index (<22) indicates fair to passable flow properties of the powder mixture [24].

### POST-COMPRESSION PARAMETERS

The physical properties of piroxicam fast disintegrating tablets are given in Table 3 and 4. In weight variation test, the pharmacopoeial limit for the tablets of not more than 7.5% of the average weight. The average percentage deviation of all tablet formulations was found to be within the above mentioned limit and hence all formulations passed the uniformity of weight as per official requirements (India Pharmacopoeia, 1996). The hardness of the

tablets was found to be in the range of 3.0±0.28 to 3.5±0.84 kg/cm$^2$. Another measure of tablets strength is friability. Conventional compressed tablets that loss less than 1% of their weight are generally considered acceptable. The percentage friability for all formulations was below 1%, indicating that the friability is within the prescribed limits. The tablets were found to contain 96.2±0.38 to 99.8±0.34 % of the labeled amount indicating uniformity of drug content.

The disintegration time of all formulations was found in the range of 32.68 ± 0.53 to 58.36 ± 0.12 sec. Among the formulations F6 and F9 showed rapid disintegration (33 sec) and all the formulations were disintegrated below 60 sec. In vitro dispersion time of formulated tablets was found in the range of 61.28±1.36 to 84.32±1.46 sec. The wetting time is closely related to the inner structure of the tablet and is mimics the action of saliva in contact with the tablet to illustrate the water uptake and subsequent wetting of tablet. The rapid wetting process in almost all formulations may be due to ability of swelling and also capacity of water absorption. The wetting time of formulated tablets was found in the range of 30.12±1.14 to 44.28±1.68 sec and water absorption ratio was 30.22 ± 1.16 to 39.46 ± 1.36. The formulated preparations were subjected for mouth feel and all were acceptable in taste. As the drug piroxicam is slightly bitter in taste, the bitter taste was masked by adding aspartame a sweetener and mannitol to give pleasant feel [25]. Thus all the formulations were with acceptable physical characteristics.

## IN-VITRO DISSOLUTION STUDY

The cumulative mean percent of piroxicam released from FDT's containing varying amounts of superdisintegrants (from F1 to F9) was found to vary from 63.9 ± 0.58 to 99.43 ± 0.29 in 15 min (Figure 1). This indicates the fast release of drug is observed from above formulations. The optimized formulations F6 and F9 showed the 99.43 ± 0.29 and 99.24 ± 0.25 drug release in the 15 min where as the conventional piroxicam tablets (control) prepared by similar manner showed 57.98±0.34 in 15 min (Figure 2). Thus the formulation F6 and F9 were considered better among other formulations to produce fast release of the piroxicam. This can be well correlated with the evaluation parameter disintegration time and wetting time which were very lower for the F6 and F9 formulations than the other formulations (Figure 3).

The percent drug release in 15 min ($Q_{15}$) and initial dissolution rate (IDR) for optimized formulations were 99.43±0.29%, 6.63%/min and 99.24±0.25%, 6.62%/min respectively. These were very much higher compared to control tablet (57.98±0.34%, 3.86%/min). The improvement in the dissolution characteristics of a drug described in terms of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 1.718 for F6 and 1.715 for F9. The DE was found to be 65.32 for F6 and 64.61 for F9 and it is increased by 3.5 fold with optimized FDT formulation compared to control tablet (Table 5). Overall increase in the dissolution performance of the optimized formulations described in terms of dissolution parameters (IDR, DE, RDR) compared to control tablet could be due to the lesser disintegration time and increased solubility of drug.

## DRUG - POLYMER INTERACTION STUDY

DSC studies were performed to understand the nature of the drug in the formulated tablets. DSC curves obtained for pure piroxicam, Sodium starch glycolate, croscarmellose sodium, crospovidone and optimized formulation (F6) were shown in figure 4. A sharp endothermic peak corresponding to the melting point of piroxicam was found at 197.41°C whereas during scanning of Sodium starch glycolate, croscarmellose sodium and crospovidone at 86.46°C, 96.11°C, 89.25°C were observed respectively.. An endothermic peak corresponding to the melting point of piroxicam in optimized formulation was observed at 197.41°C. Thermogram of the powder mixture did not show any significant shift in the endothermic peak, indicating that there was no physical change in drug in the FDT's. It is already well known that the superdisintegrants are popular in FDT's because of their compatibility with a number of drugs [26].

## CONCLUSION

Piroxicam fast disintegrating tablets were successfully formulated by employing direct compression method and found to show the significant level of drug release. From the in-vitro dissolution studies the formulations, F6 and F9 were found to be better formulations and the dissolution efficiency was increased by 3.5 fold with optimized FDT formulation compared to control tablet. DSC study showed that there is no interaction between the drug and excipients. In conclusion, development of fast disintegrating tablets using superdisintegrants is able to give rapid drug delivery and there by rapid onset of action to treat pain and inflammation.

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