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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF PIROXICAM

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ABSTRACT

Piroxicam is a non-steroidal anti-inflammatory drug, classified in the Biopharmaceutics Drug Classification system as a Class II drug with low solubility and high permeability. It demonstrates a slow and gradual absorption via the oral route and has a long half-life of elimination, rendering a prolonged therapeutic action and a delayed onset of anti-inflammatory and analgesic effect. The basic objective of the present study is to formulate and evaluate the fast dissolving tablet of Piroxicam. Study proposes the use of a Sodium Starch Glycolate (SSG) alone to prepare solid dispersion of piroxicam and comparison of its in-vitro dissolution with pure piroxicam. Fast Dissolving tablets can be prepared by conventional direct compression method using solid dispersion of superdisintegrants which shows rapid rate of disintegration. For better Hardness, less friability, faster wetting time and less moisture uptake combination of both MCC and Mannitol are required in the formulation.

Key Words: Fast dissolving tablet, Piroxicam, Sodium starch Glycolate (SSG)

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INTRODUCTION

Piroxicam is used as a first line drug in the treatment of rheumatoid arthritis and osteoarthritis and has less incidence of side effect. As Piroxicam is having half life greater than 24 hour and therefore provides more consistent analgesia than diclofenac¹. Nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used to treat patients with symptoms of acute musculoskeletal (AMS) conditions, including those associated with participation in sports². Acute musculoskeletal injuries can result in damage to soft tissue. This damage activates local inflammatory processes and leads to subsequent pain caused by inflammation. The need for relief of pain due to inflammation has led to long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) in addition to local therapy in the acute phase of injury³. Piroxicam is a non-steroidal anti-inflammatory drug that is characterized by low solubility and high permeability of the oxicam class with a prolonged serum half-life (about 50 hr). It is widely used in oral forms for chronic articular disease. Rapid onset of action and good tolerability are important properties of drugs used to treat acute musculoskeletal injuries⁴. Piroxicam is indicated for a variety of conditions requiring anti-inflammatory and/or analgesic activity, such as rheumatoid arthritis, osteoarthritis (arthrosis, degenerative joint disease), ankylosing spondylitis, acute musculoskeletal disorders and acute gout. Pain following orthopedic, dental and other minor surgery.

Due to low solubility and high permeability, its pharmacokinetic pattern is characterized by slow and gradual absorption via the oral route and a long half-life of elimination, rendering a prolonged therapeutic action but also a delayed onset of anti-inflammatory and analgesic effect. Following a single oral administration of a capsule, the maximum concentration are achieved 2hour post-dose, but this time fluctuates between 1 -6 hr and its bioavailability is between 45-75% after oral administration⁵. Because the oral mucosa is highly vascularized, drugs that are absorbed through oral mucosa directly enter the systemic circulation. Piroxicam is available in market as hard gelatin capsules and dispersible tablets. For poorly soluble, highly permeable (class II) drugs, Rate of absorption and or extent of bioavailability is controlled by rate of dissolution in biological fluid⁶. Therefore, together with permeability, the solubility and dissolution behavior of a drug are key determinants of its oral bioavailability. This undesired property, may also increase the amount of GI damage, due to long contact of drug with the mucous of GI. Thus, it is an ideal candidate for testing the potential of rapid-release without water. Piroxicam Fast Dissolving Tablet dissolves on the Tongue; this is useful for patient who can consume only small amount of liquid following surgery.

Plain piroxicam preparations are indicated for osteoarthritis and rheumatoid arthritis but not for analgesia due to its delayed onset of pain relief⁷. However, Fast Dissolving Formulation would be advantageous with regard to a rapid onset of action, especially in various painful conditions where an acute analgesic effect is desired. Hence the present work was aimed to increase rate of dissolution of piroxicam and to minimize the erratic dissolution profile of drug by applying oral cavity as route of absorption.

Oral drug delivery remains the most popular route of administration. However, limitations in the physical–chemical properties of the drug sometimes prevent a successful therapeutic outcome.

Previous studies, discussed in literature survey, have demonstrated that piroxicam, when prepared in polyethylene glycol (PEG) 4000 solid dispersion system, gave a faster dissolution than its corresponding mixtures⁸. Other studies using solid dispersions of Piroxicam in polyvinylpyrrolidone(PVP) showed significant increase in dissolution over the pure drug formulation. A recent study used gelucire 44/14 (surfactant) based solid dispersions to enhance the bioavailability of piroxicam in humans^{9, 10}. Disintegrants can help to facilitate drug dissolution and consequently can improve bioavailability. Despite use of starch as a disintegrant, it possesses disadvantages when used in direct compression formulation, the relatively high levels required and the lack of compressibility often weaken the tablet structure. Therefore in formulations for direct compression a number of disintegrants, known as superdisintegrants like cross linked carboxy methyl cellulose(Ac-di-sol.), sodium starch glycolate (Explotab) and crospovidone (polyplasdoneXL) which markedly improve tablet disintegration by swelling and exerting sufficient pressure in the tablet to break it apart into small segments.

However, not any studies found that have reported the effect of solid dispersion of Sodium Starch Glycolate on the in vitro dissolution behavior of Piroxicam. The present study proposes the use of a Sodium Starch Glycolate (SSG) alone due to its fast disintegrating action and enabling quicker hydration at room temperature. In addition, with polar head groups are more preferable due to their low toxicity, availability in pure form, stability and lower cost.

The selection of SSG was based on its swellability in aqueous and most organic solvents; furthermore, SSG's demonstrate lack of toxicity and immunogenicity.

MATERIAL AND METHODS

Piroxicam IP (Gift sample from Pure Pharma Limited, Indore), Sodium Starch Glycolate (National Chemicals, Mumbai, India), Microcrystalline Cellulose (Gift sample from Pure Pharma Limited, Indore), Colloidal silicon dioxide (Gift sample from Pure Pharma Limited,

Indore), Mannitol (Gift sample from Pure Pharma Limited, Indore), Sodium Saccharine (central drug House Ltd, Mumbai, India).

Preparation of Solid dispersion

The solid dispersions were prepared by dissolving accurately weighed quantity of Piroxicam in chloroform at room temperature and thoroughly mixing in a mortar with the Sodium starch Glycolate(SSG). The Piroxicam-SSG ratio of 1:1, 1:2, 1:3, 1:4 and 1:5 (Represented as PY-I to PY-V respectively) was used. Then chloroform was evaporated at room temperature for 30 min. and slight damp mass obtained was passed through 12 mesh which was then dried in an oven at 80°C for 2 hour. The dried mass was powdered in a mortar and passed through 60 mesh sieve and stored in tightly closed light resistant container until further use.

Evaluation of Solid dispersion

Practical Yield

Practical Yield was obtained by dividing the practical wt obtained from the sum of the weight of piroxicam and Sodium Starch Glycolate added by using following calculation

$$\% \text{ Yield} = \frac{\text{Wt of Solid dispersion}}{\text{Sum of the Piroxicam and Sodium Starch Glycolate added.}} \times 100$$

Drug Content

Accurately weighed quantity of Solid dispersions, equivalent to 20 mg piroxicam were dissolved in 100 ml of methanol by using mechanical shaker for 30 min. and filtered using what man filter paper. 1 ml of this filtrate was further diluted to 10 ml with methanol and absorbance was measured at 353 nm by UV Visible spectrophotometer.

FTIR of Solid Dispersion

FTIR Spectrum of Solid dispersion was taken from solid powder material and compared with pure piroxicam spectra by overlapping the spectra.

In vitro dissolution studies

Dissolution studies were conducted using a Type II (paddle) USP Dissolution apparatus with 650 ml Sorenson's buffer pH of 6.2 as dissolution medium. The temperature of the medium was maintained at 37.5±0.5 and RPM set as 50¹¹.

Sorenson's buffer pH 6.2 was prepared by mixing 9.25 ml of 0.2M dibasic sodium phosphate with 40.75 ml 0.2M monobasic sodium phosphate and diluted to 100 ml with double distilled water.

Comparison of *in vitro* dissolution of Pure Piroxicam and Solid dispersions

Accurately weighed amount of pure piroxicam (20 mg) was introduced into the dissolution medium (Sorensens buffer pH 6.2) and at predetermined time intervals (10 min) 10ml samples were withdrawn and then replaced with fresh dissolution medium. Samples were filtered and 1 ml of this filtrate was further diluted with methanol to 10 ml and analyzed using a UV–VIS spectrophotometer (Shimadzu UV-) at the wavelength of 353 nm. Similarly Weighed amount of solid dispersion (representing 20 mg drug) was introduced into the dissolution medium and 10 ml samples were withdrawn at predetermined time intervals (10 min.). Further dissolution study to confirm the fastest dissolution all the solid dispersions were evaluated in the 10 min run time by withdrawing samples at 1 min. time intervals.

Formulation of tablet using solid dispersion of piroxicam.

Since Solid dispersion is prepared with sodium starch glycolate, a super disintegrant, no need of addition of any other disintegrant in this formula, but binding agent may reduce the disintegration time, so a tablet with directly compressible ingredient is suitable. Microcrystalline cellulose (Avicel pH 102), which is having granular structure and providing porous structure after compression is suitable for fast disintegration as diluents. Microcrystalline cellulose alone will form a tablet with very low hardness therefore mannitol was added to improve hardness. Sodium Saccharine was used as sweetener to improve taste and glident like colloidal silicon dioxide was added to improve flow property of granules.

All ingredients were passed through mesh 60. Required quantity of each excipient was taken for particular formulation (Table 1) and the blend was mixed in double cone mixer at 30 RPM for 5 min. mixed blend of drug and excipients was compressed on single punch tablet machine using round shape biconvex punch having diameter of 9.0 mm. These tablets were dried at 45°C in oven for 30 min and stored in air tight glass container.

Table 1. Different formula for tablet Preparation

Levels	Pirox–SSG (1:4)	MCC	Mannitol	Aerosil	Sodium Saccharine.	Total weight(mg)
1 (PST 1)	106	50	12	2	1	171
a (PST 2)	106	100	12	2	1	221
b (PST 3)	106	50	62	2	1	221
ab (PST 4)	106	100	62	2	1	271

Pirox–SSG = Piroxicam: SSG Solid Dispersion. **MCC** = Microcrystalline Cellulose (Avicel pH 102). **Aerosil** = Colloidal Silicon Dioxide.

To finalize the best formula 2² Factorial design was applied on this formula to get the best result. Two factors chosen are amount of microcrystalline cellulose, and amount of mannitol. Two levels of these two are 50 mg & 100 mg for microcrystalline cellulose and 12 mg & 62 mg of Mannitol. The tablet formulations prepared by four different formula will be represented as PST 1 to PST 4 for further evaluations.

Evaluation of Fast dissolving Tablets^{12, 13}

Evaluation parameters of tablets mentioned in the pharmacopoeia need to be assessed, but some, which require special concern or need to be modified, are also discussed here.

General characteristics:

Off white, Circular shape, Biconvex tablets with bevelled edges having 9.0 mm diameter.

Content of active ingredients:

The amount of active ingredient was determined by the method described in the Drug content by crushing the 10 tablets and taking powder equivalent to 20 mg piroxicam.

Limit: Drug content should be in range of 90 to 110 % (18 -22 mg) / Tablet.

Uniformity of weight:

20 Tablets of all the batches were collected randomly during compression and weight of individual tablet was carried out.

Limit: Weight of all individual tablets should be in the limit of Average wt \pm 7.5%. Average weight was carried out by calculating the total wt. of 20 tablets (individually weighed) and dividing this value by 20.

Uniformity of content:

This test is applicable to tablets that contain less than 10 mg or less than 10% w/w of active ingredient. As this tablet is having Piroxicam 20 mg per tablet. 5 tablets of each formula were evaluated for Uniformity of Content.

Limit: Not a single tablet should go outside the limits 75 to 125% of the average value (15-25 mg)

Crushing Strength:

A significant strength of Fast dissolving tablet is difficult to achieve due to the specialized processes and ingredients used in the manufacturing. The limit of crushing strength for an FDT is usually kept in a lower range to facilitate early disintegration in the mouth. The crushing strength of the tablet may be measured using conventional hardness testers.

Friability:

To achieve % friability within limits for an FDT is a challenge to the formulator since all methods of manufacturing of FDT are responsible for increasing the % friability values. Thus, it is necessary that this parameter should be evaluated and the results are within bound limits (0.1 to 0.9%).

This test was carried out by using Tablet Friability test apparatus (Scientific). Twenty preweighed tablets were rotated at 25 rpm for 4 minutes. The tablets were then reweighed after removal of fines (using no. 60 mesh screen), and the percentage of weight loss was calculated using the following formula.

$$\% \text{ friability} = \frac{\text{Wt. of 20 tablets before rotation} - \text{Wt. of 20 tablets after rotation}}{\text{Wt of 20 tablets before rotation}} \times 100$$

Wetting time:

Wetting time of dosage form is related with the contact angle. Wetting time of the Fast Dissolving Tablets is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet.

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Modified disintegration test:

The time for disintegration of Fast Dissolving Tablets is generally less than one minute. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for FDT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of Petri dish and the time for the tablet to completely disintegrate into fine particles was noted.

Dissolution test:

The development of dissolution methods for Fast Dissolving Tablets is comparable to the approach taken for conventional tablets, and is practically identical. Test was carried out according to the In vitro dissolution test using Tablet in Sorenson's buffer pH 6.2.

Moisture uptake studies:

Moisture uptake studies for Fast Dissolving Tablets should be conducted to have an insight into the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets were then weighed and exposed to 75% RH, at room temperature for one week. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for three days. Tablets were weighed and the percentage increase in weight was recorded daily.

Factorial Design and Optimization:

Factorial Design

Factorial design is a system of experimental design which provides a means whereby the factors involved in a reaction or a process can be evaluated simultaneously and their relative importance assessed. It is thus a means of separating those factors which are important from those which are not. Factorial design involves the variation of two or more levels. The technique establishes the relative order of importance of the factors, and can also indicate if factors interact and if such interactions are significant.

Optimization:

Many Pharmaceutical formulations and processes lend themselves to optimization procedures, whereby the best possible result is sought, given a series of limits or constraints. Thus the best possible solution is not necessarily a maximum (or minimum) value, but is rather a compromise, taking a number of factors into account.

Optimization has been defined as the implementation of systematic approaches to achieve the best combination of product and/or process characteristics under a given set of conditions¹⁴.

There are two principle methods of Optimization.

1. Model Dependent optimization, in which a group of experimentation is carried out and the result then fitted to an equation (the model). Adequate experimental design, usually factorial in nature is prerequisite for this type of model. Here a series of experiments be carried out and the results assessed only when the whole series has been completed.
2. The other method is Model independent method by which the results assessed of only a few experiments govern the condition of further experiments.

Model dependent Optimization of Formula for preparation of Piroxicam Fast dissolving Tablet

In this design, concentration of directly compressible material microcrystalline cellulose (Avicel pH 102) and concentration of Mannitol are the independent variables. The evaluated parameters were taken as dependent variables. Their magnitudes are governed by the values of independent variables.

The first stage of process is to obtain experimental data, and this is best achieved by means of a two-factor, two-level factorial design.

Two – factor, two-level experimental design

The most frequent encountered notation for two level studies was used.

Factor A= Amount of Microcrystalline cellulose

(50 mg = low level, 100 mg = High level)

Factor B= Amount of Mannitol

(12 mg = Low level, 62 mg= High Level)

Obtaining a Polynomial Equation

The next stage in the optimization procedure is to carry out multiple regression analysis. This involve fitting the values of a dependent variable and the independent variables in to polynomial equation of the form-

$$Y = B_0 + B_1X_1 + B_2X_2$$

Where Y= Dependent variable

B₀, B₁ and B₂ = Coefficients

The values of coefficients (B₀, B₁ and B₂) were obtained by multiple regression analysis by using Computer program in BASIC command.

RESULTS AND DISCUSSION

Solid Dispersion

Practical Yield

The percentage yield of solid dispersion are shown in Table 2

Table 2. Formula of Solid dispersions in different ratios with Practical Yield

Formula	Piroxicam(g)	SSG(g)	Theoretical yield(g)	Practical yield (g)	%Yield
PY -I	1	1	2	1.94	97.20
PY -II	1	2	3	2.95	98.46
PY -III	1	3	4	3.92	98.05
PY -IV	1	4	5	4.89	97.84
PY -V	1	5	6	5.91	98.50

Drug content

Prepared solid dispersions were evaluated for drug content. The results obtained are shown in Table 3.

Table 3. Drug content of Solid dispersions

Formula	Weight. Taken	Practical Yield(mg)	Abs of Standard	Abs of Sample	Drug content	Weight Required
PY -I	40	1944	0.485	0.843	844.73	46.02
PY -II	60	2954	0.485	0.769	780.62	75.68
PY -III	80	3922	0.485	0.879	888.51	88.28
PY -IV	100	4892	0.485	0.907	878.54	106.82
PY -V	120	5910	0.485	0.831	843.85	140.07

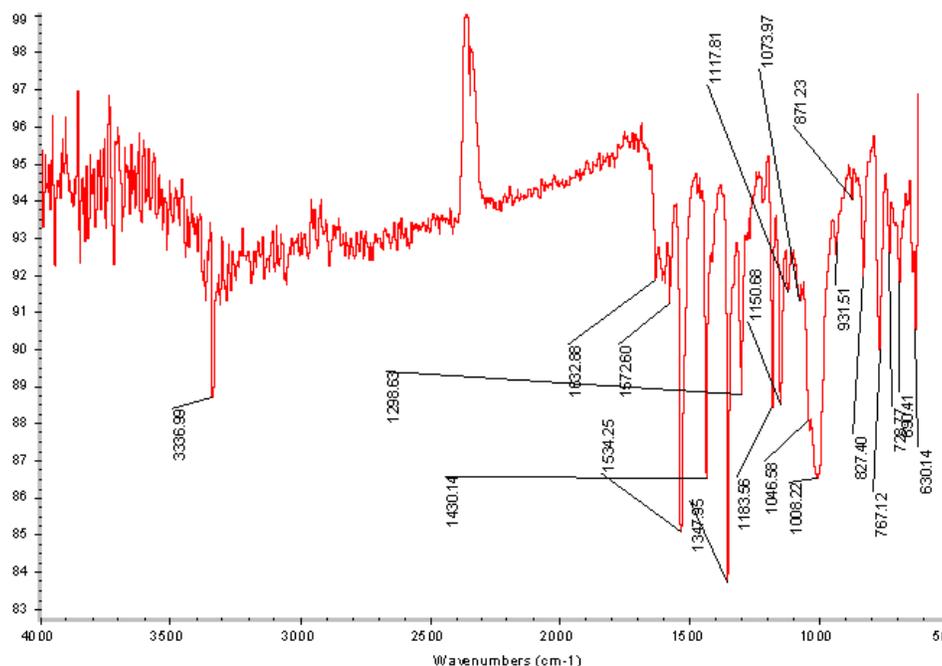
Weight Taken= Theoretical wt. of Solid dispersion equivalent to 20 mg Piroxicam

Drug Content= Content of Piroxicam in mg / Practical yield

Weight Required=Weight of Solid dispersion required equivalent to 20 mg Piroxicam

FTIR of Solid dispersion

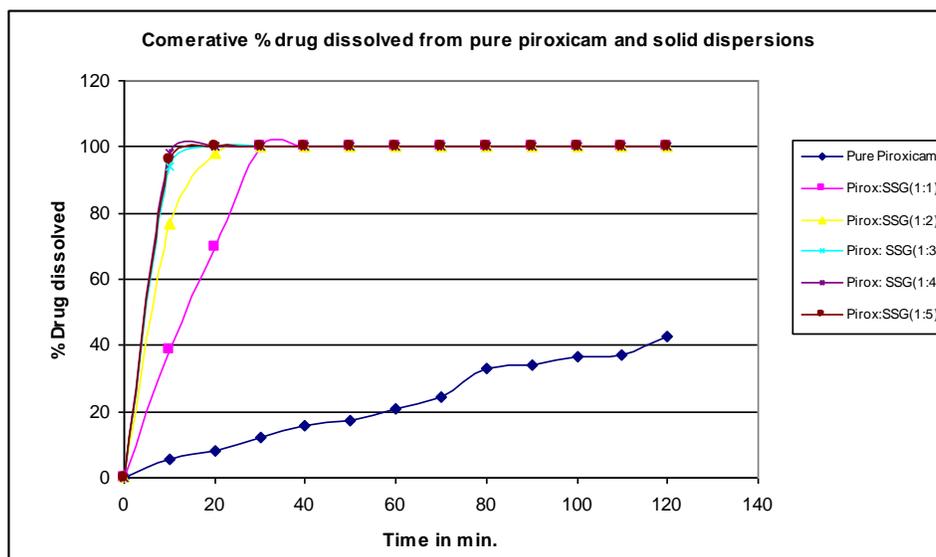
FTIR Spectra of Solid dispersions displayed broad peak at about 1008 cm⁻¹. In spite of this broad peak, the FTIR spectra of solid dispersion still showed peak of N-H or O-H stretching vibration of Piroxicam at 3391cm⁻¹. This indicates that solid dispersion spectra were only the summation of piroxicam and SSG spectra and reflected that there was no major interaction between Piroxicam and SSG. (figure 1)

**Figure 1. FTIR spectrum of Solid dispersion**

***In vitro* dissolution studies**

In dissolution study, the initial % drug dissolved in 2 hour was examined by plotting % drug dissolved in Sorenson's buffer pH 6.2 against a function of time. Piroxicam alone yielded the slowest dissolution with only 42.73% drug was dissolved in 2 hour run time. The dissolution was found significantly faster when evaluated with solid dispersion of SSG, in different ratio. Formulation PY-IV and PY-V showed the fastest dissolution with the entire drug amount released within 7 min of the 10 min.

Since SSG in 1:4 and 1:5 were found to have similar results, the formula with lesser amount (1:4) of SSG was selected to be incorporated in tablet formulation. (Figure 2&3)



**Figure 2. Comparative % drug dissolution from Pure Piroxicam and Solid dispersions
Tablet Formulation**

First table formulation was developed from piroxicam-SSG (1:4) solid dispersion using Microcrystalline Cellulose as diluent. The tablet was found to have very less hardness, therefore other excipients were evaluated for formulation of tablet like Mannitol, which gives some better strength but longer disintegration time in comparison to tablet prepared only with MCC, so the mixture of both was selected to be added to formulate a tablet by direct compression that give better hardness and fast disintegration by direct compression in different proportions and evaluated.

Table 4 shows the general characteristics in the form of shape and size of tablets of all the four different formulations and found satisfactory. Drug content per tablet is also well within the pharmacopoeial specification. Uniformity of weight was evaluated by using 20 tablets of each

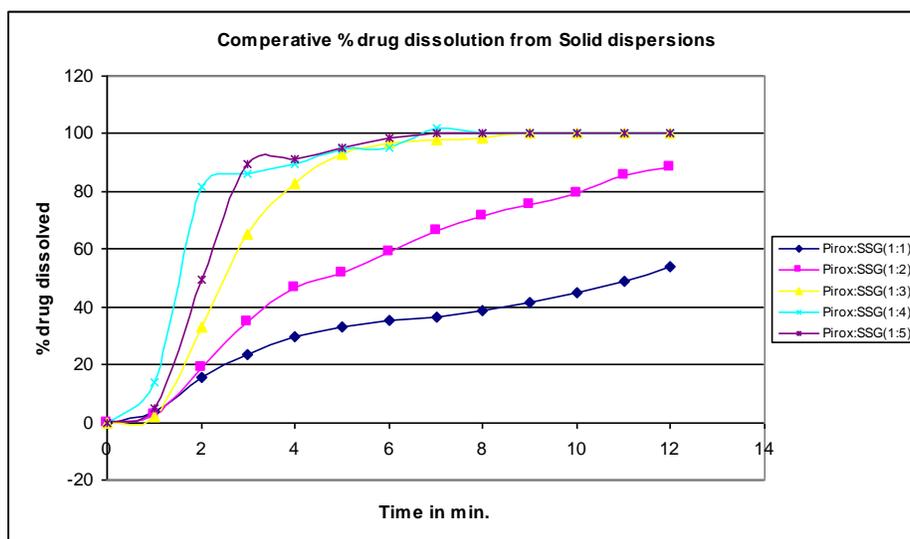


Figure 3. Comparative % drug dissolution from Solid dispersions

formula and also found complying according to pharmacopoeial limit as shown in Table 4. Since the active ingredient piroxicam is present in the Tablet in concentration range near to 10% of total tablet weight content uniformity of tablet is an important parameter evaluated on 5 tablets of each formulation and found Suitable according to limit in Table 4.

Table 4. Characteristics of tables

Properties	PST - 1	PST - 2	PST - 3	PST - 4
Description	Off white, Circular shape, Biconvex tablets with bevelled edges having 2.0 ± 0.2 mm Thickness and 9.0 ± 0.2 mm Diameter	Off white, Circular shape, Biconvex tablets with bevelled edges having 2.15 ± 0.2 mm Thickness and 9.0 ± 0.2 mm Diameter	Off white, Circular shape, Biconvex tablets with bevelled edges having 2.15 ± 0.2 mm Thickness and 9.0 ± 0.2 mm Diameter	Off white, Circular shape, Biconvex tablets with bevelled edges having 2.20 ± 0.2 mm Thickness and 9.0 ± 0.2 mm Diameter
% Drug Content	95.37 ± 2.15	93.475 ± 3.56	95.74 ± 3.89	95.38 ± 2.65
Hardness (kg / cm²)	1.33 ± 0.44	1.83 ± 0.76	2.66 ± 0.54	2.83 ± 0.97
Friability (%w/w)	4 ± 0.57	2 ± 0.87	1.2 ± 0.32	1.4 ± 0.64
Wetting time(sec.)	64 ± 3	73.2 ± 6	73.4 ± 5	76.4 ± 4
Disintegration time(sec.)	54 ± 5	65 ± 3	70 ± 4	67 ± 6
% Moisture Uptake	26 ± 3	27 ± 4	18 ± 5	21 ± 4

Hardness of tablets is one of the important parameter and Tablets should be hard enough to withstand during handling during operation, packaging and transportation. But the tablets

prepared here by direct compression method resulted in tablets with very low friable and highly hardness as shown in Table 4. Wetting time and modified disintegration time, which are the important criteria for determining the capacity of disintegrates to swell in presence of little water were found between 64 to 76 seconds and 54 to 70 seconds respectively (Table 4). Moisture uptake was also found higher in 26% for formula PST-1 and lower upto 18 % in PST-3 (Table 4)

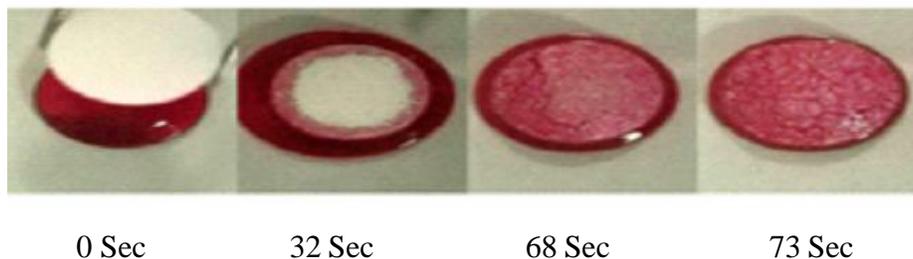


Figure 4. Wetting time of Tablets

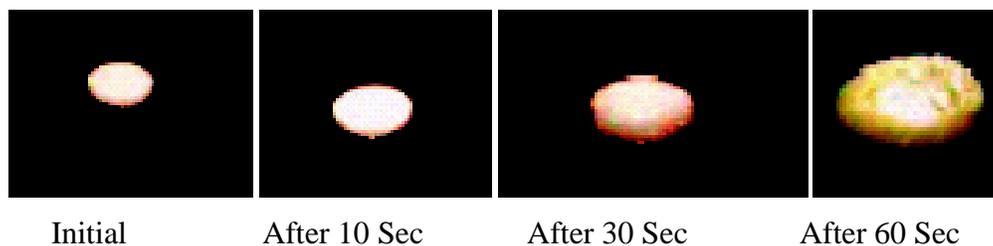


Figure 5. Modified Disintegration Time of Tablet

Factorial Design

Two factors two level factorial designs was applied on this formula to find the effect of independent variables on dependent variables and polynomial equation was derived for evaluate the effects of these variables.

The effect of individual factors and effect of interaction were carried out by following formula. Effect of MCC was determined from $\frac{1}{2}\{(a+ab)-(1+b)\}$, Effect of Mannitol was determined from $\frac{1}{2}\{(b+ab)-(1+a)\}$, Effect of Interaction was determined from $\frac{1}{2}\{(1+ab)-(a+b)\}$.

From the results of factorial design it was found that the Interaction of microcrystalline cellulose and Mannitol is not found for Crushing strength and Moisture absorption because the data presented graphically shoeing two virtually parallel lines. This indicates that there is no significant interaction between the two independent variables and both independent variables significantly affect the response. But all other parameters evaluated are affected by presence of both microcrystalline cellulose and Mannitol in the Formula because the lines obtained are not parallel.

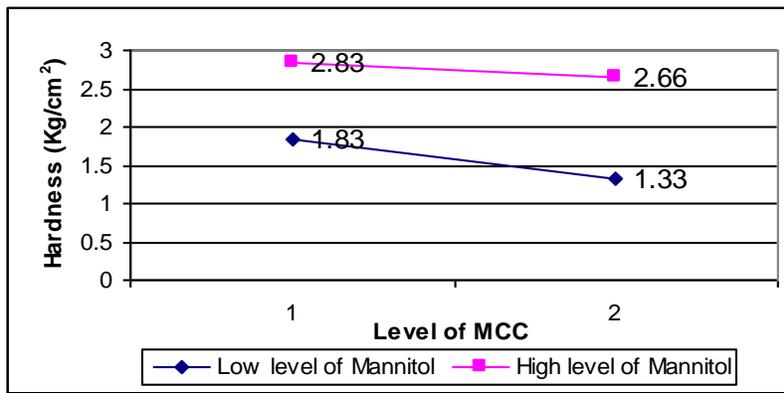


Figure 6. Comparative Effect of Variables on Hardness

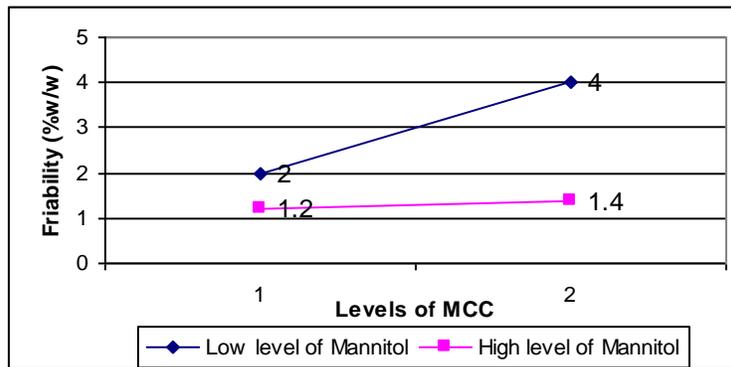


Figure 7. Comparative Effect of Variables on Friability

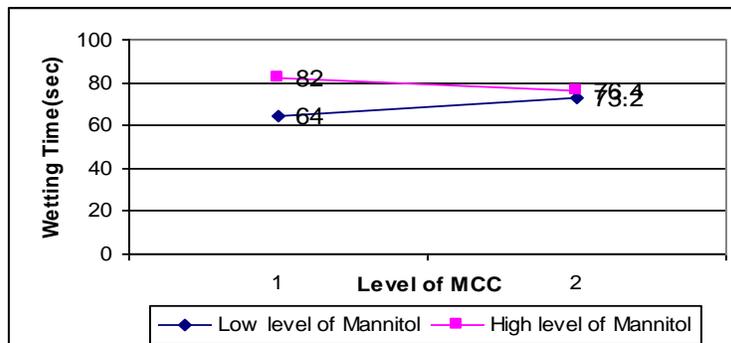


Figure 8. Comparative Effect of Variables on Wetting time

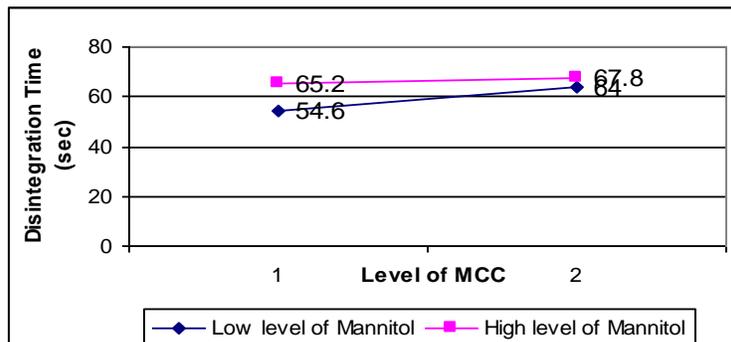


Figure 9. Comparative Effect of Variables on Disintegration time

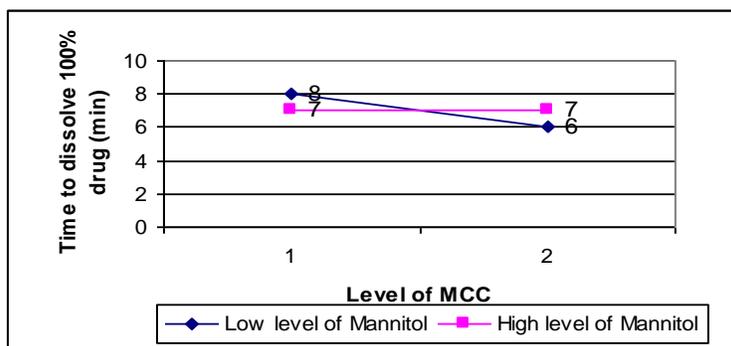


Figure 10. Comparative Effect of Variables on Dissolution time

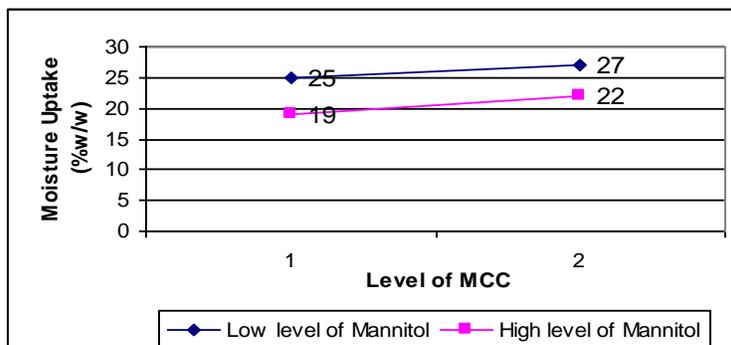


Figure 11. Comparative Effect of Variables on Moisture Uptake

Polynomial Equations for -

1.Hardness

$$Y=1.803 - 0.007X_1 + 0.023X_2$$

2.Friability

$$Y=1.758 + 0.022X_1 - 0.034X_2$$

3.Wetting Time

$$Y=63.356 + 0.036 X_1 + 0.212 X_2$$

4.Disintegration

$$Y=45.77 + 0.174 X_1 + 0.09 X_2$$

5.Dissolution

$$Y=8.5 - 0.02 X_1 + 0$$

6.Moisture uptake

$$Y= 25.18 + 0.04 X_1 - 0.14 X_2$$

All these equation shows the sign with the coefficient of independent variable according to the effect of that particular independent variable on dependent variable as positive or negative. The value of any one variable can be obtained from the polynomial equations according to required

characteristic, if the value of other variable and value of Dependent variable to be fixed is known.

Eg. If Tablet to be produced with Hardness of 5 kg/cm^2 with 100 mg of MCC amount of Mannitol required is =

$$5 = 1.803 - 0.007 (100) + 0.023 X_2$$

$$X_2 = (5 - 1.803 + 0.7) / 0.023$$

168 mg of mannitol

Fast Dissolving tablets gets Dissolved / disintegrated in mouth quickly which can be easily swallowed. This characteristic feature is useful for patient compliance. The time required for complete wetting was few seconds hence tablets disintegrate rapidly in oral cavity. Thus the release rate of piroxicam can be significantly enhanced by rapidly disintegrating superdisintegrants.

As piroxicam is an acidic drug with pKa (acidity) 6.3 in dioxane and water (2:1)¹⁵ can be ionized as a zwitterions that has two pKa 1.86 and 5.46. This indicates High amount of Piroxicam will remain in the dissociated forms at pH range near to pKa. But it is having a partition coefficient of 1.8 between n-octanol and aqueous buffer pH 7.4¹⁵. This indicates the drug is highly Hydrophobic in nature and will be absorbed fastly through mucosal membrane once it is solubilized. From Acidity (pKa) and Partition coefficient Values, Piroxicam is found to be suitable to formulate in complex formation to improve solubility in Sorenson's Buffer pH 6.2.

Poor solubility of Piroxicam can be attributed to its hydrophobic nature, poor wettability and evidence of particle agglomeration during the dissolution. Improvement in Dissolution with SSG Solid dispersions must be due to the increased wettability, decreased particle size of drug and prevention of the aggregation of drug.

Since results of Dissolution of Tablets were found similar to that of Solid dispersions indicates the addition of Microcrystalline cellulose (Avicel pH 102) to the Solid dispersion afforded a greater wetting effect on the drug Formulation after compressing the Solid dispersion and thus enhancing the Disintegration and dissolution rate by rapid swelling without destruction of contact with water. The presence of Mannitol, creates a better micro-environment for the dissolution of the drug and provide better compressibility of the Formulation. As mannitol is not hygroscopic in nature, so suitable for stability of formulation containing moisture sensitive MCC. In this case, the presence of SSG with MCC and Mannitol showed over an increase in Hardness compared to that only with MCC. Formulations 'b'(PST-3) and 'ab'(PST-4) exhibited

intermediate dissolution characteristics and showed no significant difference in dissolution time but formulation 'a'(PST 2) having lesser amount of Mannitol and higher amount of MCC showed fastest release. The friability results were found as out of specification, which should be improved. The environmental conditions must have very less humid and dry atmosphere to formulate these tablets because of moisture sensitive MCC and SSG in the formulation. Aerosil did not represent any distinct advantage over formulation. But for better flow of directly compressible powder blend aerosil was added. From the all results of 22 factorial design it was found that microcrystalline cellulose reduces the hardness, increase friability, reduce wetting time, disintegration time and dissolution time, and increase moisture uptake. While Mannitol increase hardness, reduce friability, increase wetting time, disintegration time and reduce moisture uptake. For formulation and storage of this type of Tablet Relative humidity of area should be maintained below 30% RH. For storage of final product Packaging material and design of packaging is needed much attention because of Highly Friable and Moisture sensitive Dosage form.

From the present study it may be concluded that Fast Dissolving tablets can be prepared by conventional direct compression method using solid dispersion of superdisintegrants which shows rapid rate of disintegration. For better Hardness, less friability, faster wetting time and less moisture uptake combination of both MCC and Mannitol is required in the formulation. It concludes Formula having 100 mg MCC and 62 mg Mannitol is suitable as Fast dissolving Tablet. Though the main effect is release of drug was best in formulation containing 100 mg MCC and 12 mg Mannitol but the selection of formula for tablet formulation will depend on other characteristics also which indicate the formula with 100 mg MCC and 62 mg Mannitol is suitable for tablet as result of release study is not varying at much extent.

CONCLUSION

From the results obtained, it can be concluded that the solid dispersion of Piroxicam - SSG markedly improved the dissolution of piroxicam powder. Tablets with MCC and Mannitol showed the better dissolution rate from formulation. The physical properties of all prepared tablets formulation were acceptable according to parameters of Fast dissolving Tablet. The disintegration time value for Piroxicam tablets containing SSG prepared using the MCC and mannitol was the faster enough as compared to conventional tablet dosage form.

Since in these formulation SSG included in solid dispersion form is found in much higher concentration than the general concentration of superdisintegrant in other Tablet dosage form.

These may cause incompatibility during usage by Patients, so further research work is needed by replacing the same amount of SSG with other superdisintegrant in acceptable range.

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