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Original Research Article

POLOXAMER 188 USED AS WATER SOLUBLE CARRIER FOR ENHANCED DISSOLUTION RATE OF PIROXICAM BY SOLID DISPERSION TECHNIQUE

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Abstract: Piroxicam is a long acting potent Non-Steroidal anti inflammatory drug with inflammatory potency and good analgesic-antipyretic action. It is a reversible inhibitor of COX lowers PG concentration in synovial fluid and inhibits platet aggregation prolonging bleeding time. In addition it decreases to IgM rehumatoid factor and leucocyte chemotaxis. Thus it can inhibit inflammation in diverse ways. It is practically insoluble in water and a biopharmaceutics classification system class II drug and exhibits a slow rate of dissolution in aqueous media, resulting in its poor oral bioavailability. Solid dispersion is widely used to increase the dissolution rate, and hence improving the bioavailability of poorly water soluble drugs. It is still a challenge for the formulation scientists to develop an oral dosage form of Piroxicam having a faster rate of dissolution. The present research work was aimed to develop a fast dissolving oral dosage form of Piroxicam for enhancing its bioavailability. The solid dispersion of Piroxicam was prepared by solvent evaporation technique using Poloxamer 188 as a carrier. The fast dissolving tablet of Piroxicam were developed using Piroxicam-Poloxamer 188 solid dispersion. The developed tablets of solid dispersion exhibited about a 10 fold enhancement in the dissolution rate resulting upto 98% drug release in 1hr. The problem of poor dissolution of Piroxicam could be successfully resolved through solid dispersion technique using Poloxamer 188 as a carrier. Procured drug sample of Piroxicam was characterized by melting point determination XRD and UV spectroscopy. The prepared solid dispersion was characterized using powder XRD techniques. The findings demonstrate that poloxamer 188 can successfully resolve the problem of slow dissolution and poor bioavailability of Piroxicam through solid dispersion approach.

Key Words:- Solid Dispersion, Dissolution Rate, Poloxamer 188, Piroxicam, Bioavailability.

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1. Introduction

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. In addition, the oral medication is generally considered as the first avenue investigated in the discovery and development of new drug entities and

pharmaceutical formulations, mainly because of patient acceptance, convenience in administration, and cost-effective manufacturing process.[1]

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in body to achieve and maintain the desired drug concentration. That is, the drug delivery system should deliver drug at a rate dictated by the needs of the body over the period of treatment.[2]

Despite tremendous advancement in diverse drug delivery approaches, the oral route remains the most acceptable route of drug administration because of low cost of therapy, ease of administration, and improved patient compliance Thus, the oral solid dosage forms are the most widely used formulations for new and existing modified release (MR) products.[3]

1.1 Modified-Release Drug Products[4]

- Extended-release drug products
  A dosage form that allows at least a twofold reduction in dosage frequency as compared to an immediate-release (conventional) dosage form. Examples of extended-release dosage forms include sustained-release, and long-acting drug products.
- Delayed-release drug products
  A dosage form that releases a discrete portion or portions of drug at a time or at times other than promptly after administration, although one portion may be released promptly after administration. Enteric-coated dosage forms are the most common delayed-release products.
- Targeted drug delivery products
  A dosage form that releases drug at or near the intended physiologic site of action. Targeted-release dosage forms may have either immediate- or extended-release characteristic.
- Controlled-release drug products
  The controlled release products delivers the drug at a predetermined rate and /or to a location according to the needs of the body and disease for a definite time period.
- Fast-release drug products
  Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such fast-release system results in relatively rapid drug absorption and fast onset of action. There have been a number of formulation approaches explored and widely practiced in the pharmaceutical industry to improve delivery of poorly water soluble compounds especially in development of fast release dosage forms. These delivery approaches are based on various techniques, such as

- Particle size reduction
- Solid dispersion
- Formation of the salt and polymorphs
- Use of co-solvent
- Complexation with the excipients such as cyclodextrin

Together with the permeability, the solubility behavior of drug is key determinant of its oral bioavailability. There have always been drugs for which solubility has presented a challenge for the development of a suitable formulation for oral administration. Solid dispersion techniques are particularly promising for improving the oral absorption and bioavailability of BCS Class II drugs.[5]

1.2 Biopharmaceutical Classification System[6]

The BCS is a scientific framework for classifying drug substances based on their aqueous solubility and permeability. The BCS can be used as a drug development tool to justify request for biowaivers.

1.3 Solid Dispersion[7]

Solid dispersions have been widely used to increase the dissolution rate, and hence improving the bioavailability of poorly water soluble drugs. They are defined as a dispersion of one or more active ingredients in an inert carrier or matrix in the solid state. Usually, a drug substance is incorporated into a water-soluble polymer, leading to a molecular, a

crystalline or an amorphous dispersion of the drug. Although the metastable drug form dissolves faster than the crystalline state, the dissolution rate depends on the drug–polymer ratio.

1.4 Generation of Solid Dispersions[8]

1.4.1 First Generation Solid Dispersions

Crystalline carriers include urea and sugars, which were the first carriers to be employed in solid dispersions. They have the disadvantage of forming crystalline solid dispersions, which were more thermodynamically stable and did not release the drug as quickly as amorphous ones.

1.4.2 Second Generation Solid Dispersions

A second generation of solid dispersions appeared, containing amorphous carriers instead of crystalline. Polymeric carriers have been the most successful for solid dispersions, because they are able to originate amorphous solid dispersions. These systems are able to reduce the drug particle size to nearly a molecular level, to solubilize or co-dissolve the drug by the water soluble carrier, to provide better wettability and dispersibility of the drug by the carrier material, and to produce amorphous forms of the drug and carriers. In these solid dispersions, the carrier dissolution (or mixtures of carriers) dictates the drug release profile.

1.4.3 Third Generation Solid Dispersions

Recently, it has been shown that the dissolution profile can be improved if the carrier has surface activity or self-emulsifying properties, therefore third generation solid dispersions appeared. These contain a surfactant carrier, or a mixture of amorphous polymers and surfactants as carriers. These third generation solid dispersions are intended to achieve the highest degree of bioavailability for poorly soluble drugs and to stabilize the solid dispersion, avoiding drug re-crystallization.

1.5 Methods For Preparation of Solid Dispersions[9]

Melting and solvent evaporation methods are the two major processes of preparing solid dispersions.

1.5.1 Melting Method

In this method, the drug is mixed with the carrier and heated slightly above the melting point of the highest melting solid until a clear liquid is formed. The liquid is allowed to solidify and subsequently pulverized into a powder of a particular sieve size range usually 125-250µm. Several modifications, like hot-stage extrusion MeltrexTM or melt agglomeration were introduced to the original method[10].

- Hot-stage extrusion

  Hot-stage extrusion consists of the extrusion, at high rotational speed, of the drug and carrier, previously mixed, at melting temperature for a small period of time. The resulting product is then collected after cooling at room temperature and milled. A reduction in processing temperature can be achieved by the association of hot-stage extrusion with the use of carbon dioxide as a plasticizer which broadens the application of hot-stage extrusion to thermally labile compounds. Solid dispersions of p-aminosalicylicacid/ ethylcellulose, itraconazole /PVP and itraconazole /ethyl cellulose were successfully prepared by this technique[11].

- Meltrex^{TM}

  Meltrex^{TM} is a patented solid dispersion manufacturing process, also on the basis of the melting process. The crucial elements in the Meltrex^{TM} technology is the use of a special twin screw extruder and the presence of two independent hoppers in which the temperature can vary over a broad temperature range. This process permits a reduced residence time of the drug in the extruder, allowing a continuous mass flow and avoiding thermal stress to the drug and excipients. Additionally, it is possible to use the application of this technique to protect drugs susceptible to oxidation and hydrolysis by complete elimination of oxygen and moisture from the mixture[12].

- Melt agglomeration

  This method allows the preparation of solid dispersions in conventional high shear mixers. The solid dispersion is made by adding the

molten carrier containing the drug to the heated excipients, by adding the molten carrier to a heated mixture of drug and excipients or by heating a mixture of the drug, carrier and excipients to a temperature within or above the melting range of the carrier. It is also possible to produce stable solid dispersions by melt agglomeration in a rotary processor.

- Fusion method

The fusion method is sometimes referred to as the melt method, which is correct only when the starting materials are crystalline. Therefore, the more general term fusion method is preferred. The first solid dispersions created for pharmaceutical applications were prepared by the fusion method. The dispersion consisted of sulfathiazole and urea as a matrix which were melted using a physical mixture at the eutectic composition, followed by a cooling step[13].

1.5.2 Solvent Evaporation Method

The solvent evaporation method consists of the solubilization of the drug and carrier in a volatile solvent that is later evaporated. In this method, the thermal decomposition of drugs or carriers can be prevented, since organic solvent evaporation occurs at low temperature. In this method the drug and the carrier both are dissolved in a common solvent and then the solvent is evaporated under vacuum to produce a solid solution. An important prerequisite for the manufacture of a solid dispersion using the solvent method is that both the drug and the carrier are sufficiently soluble in the solvent. The solvent can be removed by any one of a number of methods. Temperature used for solvent evaporation usually lies in the range of 23 $\pm$ 6.5 °C. The solvent can also be removed by freeze-drying. Differences in solvent evaporation processes are related to the solvent evaporation procedure, which usually include vacuum drying, heating of the mixture on a hot plate, slow evaporation of the solvent at low temperature, the use of a rotary evaporator, a stream of nitrogen, spray-drying, freeze-drying and the use of supercritical fluids (SCF)[14].

- Spray-drying

Spray drying is one of the most commonly used solvent evaporation procedures in the production of solid dispersions. It consists of dissolving/suspending the drug and carrier, then spraying it into a stream of heated air flow to remove the solvent.

- Freeze-drying process

The basic freeze-drying process consists of dissolving the drug and carrier in a common solvent, which is immersed in liquid nitrogen until it is fully frozen. Then, the frozen solution is further lyophilized. Van drooge et al[11], prepared an alternative solid dispersion by spraying a povidone and diazepam solution into liquid nitrogen, forming a suspension that was then lyophilized.

- Supercritical fluid methods

Supercritical fluid methods are mostly applied with carbon dioxide (CO2), which is used as either a solvent for drug and matrix or as an anti-solvent. When supercritical CO2 is used as solvent, matrix and drug are dissolved and sprayed through a nozzle, into an expansion vessel with lower pressure and particles are immediately formed. The adiabatic expansion of the mixture results in rapid cooling. This technique does not require the use of organic solvents and since CO2 is considered environmentally friendly, this technique is referred to as 'solvent free'. The technique is known as Rapid Expansion of Supercritical Solution (RESS). However, the application of this technique is very limited, because the solubility in CO2 of most pharmaceutical compounds is very low (<0.01wt-%) and decreases with increasing polarity. Therefore, scaling up this process to kilogram-scale will be impractical[15].

- Co-precipitation method

Another common process is the co-precipitation method, in which a non-solvent is added dropwise to the drug and carrier solution, under constant stirring. In the course of the non-solvent addition, the drug and carrier are co-precipitated to form micro-particles. At the end,

the resulted microparticle suspension is filtered and dried[16].

- Spin-coated films

Spin-coated films is a new process to prepare solid dispersions by the solvent evaporation method, which consists of dissolving drug and carrier in a common solvent that is dropped onto a clean substrate highly spinned. Solvent is evaporated during spinning. This process is indicated to moisture sensitive drugs since it is performed under dry conditions[17].

1.6 Pharmaceutical Applications of Solid Dispersions[18]

- Solid dispersions can be used to increase the dissolution and absorption of poorly water soluble drugs.
- To stabilise unstable drugs, many drug molecules can be protected by a solid inclusion against hydrolysis, oxidation, racemisation, isomerisation, photo oxidation and other decomposition processes.
- To obtained a homogenous distribution of a small amount of drug in solid state.
- To formulate a fast release priming dose in a sustained release dosage form.
- To formulate sustained release or prolonged release regimens of soluble drug by using poorly soluble and insoluble carriers.

2. Materials and Methods

2.1. *Materials*

Piroxicam is a drug of the oxicam class, it was purchased from Sun pharmaceuticals Ltd, Mumbai. it is chemically (8*E*)-8-[hydroxy-(pyridin-2-ylamino)methylidene]- 9-methyl-10,10-dioxo-10λ^6-thia-9-azabicyclo[4.4.0] deca-1,3,5-trien-7-one.[19] Poloxamer 188 was kindly provided by BASF India (Mumbai). All reagents and solvents used were of analytical grade.

2.2 Methods

2.2.1 Determination of Melting Point of Piroxicam

The melting point of piroxicam was determined using open capillary method. The capillary filled with drug powder was placed in a Thiel's tube containing liquid paraffin. The tube was heated and the melting point of drug powder was noted.

2.2.2 Preparation of Calibration Curve:

2.2.2.1 Calibration Curve of Piroxicam in Ethanol:

Accurately weighed quantity of piorxicam (10 mg) was dissolved in about 80 ml of ethanol in 100 ml volumetric flask and volume was made upto 100 ml by ethanol. Aliquots of the above solution were taken and diluted to get piorxicam concentration in the range of 5-30 µg/ml. The resulting dilutions were analysed at 345 nm on Shimadzu-1800 UV spectrophotometer against ethanol blank. The absorbance data are shown in the table no. 1 and graphically represented in fig 1.

2.2.2.2 Calibration Curve of Piroxicam in Simulated Gastric Fluid P^H 1.2 at 342 nm

Accurately weighed quantity of piorxicam (10 mg) was dissolved in about 80 ml of Simulated Gastric Fluid P^H 1.2 in 100 ml volumetric flask and volume was made upto 100 ml by Simulated Gastric Fluid P^H 1.2. Aliquots of the above solution were taken and diluted to get piorxicam concentration in the range of 5-30 µg/ml. The resulting dilutions were analysed at 342 nm on Shimadzu-160A UV spectrophotometer against Simulated Gastric Fluid P^H 1.2 solution blank. The absorbance data are shown in the table 2 and graphically represented in fig. 1

2.2.3 Selection of Carrier for Preparation of Solid Dispersion

Solid dispersions of piroxicam with various carriers in different ratio were prepared Solid dispersions of piroxicam with water soluble carrier using different ratio. In this method the drug and the carrier both are dissolved in a common solvent and then the solvent is evaporated under vacuum to produce a solid solution. An important prerequisite for the manufacture of a solid dispersion using the solvent method is that both the drug and the carrier are sufficiently soluble in the solvent. Temperature used for solvent evaporation usually lies in the range of 23 $\pm$ 6.5 °C. This

solution was dried in a tray dryer. Each of the solid dispersion was compressed into a tablet and subjected to dissolution rate study.

The dissolution rate study was performed using USP (type II) Electrolab dissolution apparatus. The rpm of paddle was fixed at 50 rpm. and simulated gastric fluid P^H 1.2 solution was used as dissolution media at temperature of 37±0.5 ^{0}C. The samples of dissolution fluid were withdrawn at different time intervals, diluted suitably and analyzed for drug content. Withdrawn samples were replaced with equal volume of after each withdrawal. The results of dissolution studies are shown in table no. 3 and graphically represented in fig. 2.

2.2.4 Drug-Excipient Physical Compatibility Study

This study was performed to determine any physical change in the drug when kept in contact with various excipients. Drug and excipients were mixed in the ratio as presented in table 6.3. The control samples containing drug without excipient were sealed in vials and the samples were withdrawn every week till one month and observed for any physical incompatibility like change in color and physical state. The observations are recorded in table no. 4.

2.2.5 Determination of Excipient Interference in UV Spectrophotometric Analysis of Piroxicam

2.2.5.1 Determination of Excipient Interference in Analysis in Ethanol

Ten mg of poloxamer 188 were added separately to 100 ml volumetric flask and volume was made upto 100 ml with ethanol. These flasks were shaken and then filteration was done. Ten mg of drug was dissolved in ethanol in 100 ml volumetric flask and volume made upto the mark with ethanol to obtain a stock solution of 100 µg/ml. Then, 1 ml of drug stock solution was added separately to 10 ml volumetric flask and volume was made upto the mark with ethanol. Then, 1 ml of drug stock solution and 1 ml of each excipient stock solution (filtered) was added in another 10 ml volumetric flask and volume was made upto the mark with ethanol. The samples were analyzed at 345 nm against ethanol. The results are recorded in table 5.

2.2.5.2 Determination of Excipient Interference in Analysis in Simulated Gastric Fluid P^H 1.2

Ten mg of poloxamer-188 and 50 mg of all other tablet excipients were added separately to 100 ml volumetric flask and volume was made upto 100 ml with simulated gastric fluid P^H 1.2. These flasks were shaken and then filteration was done. Ten mg of drug was dissolved in simulated gastric fluid P^H 1.2 in 100 ml volumetric flask and volume made upto the mark with simulated gastric fluid P^H 1.2 to obtain a stock solution of 100 µg/ml. Then, 1 ml of drug stock solution was added separately to 10 ml volumetric flask and volume was made upto the mark with simulated gastric fluid P^H 1.2. Then, 1 ml of drug stock solution and 1 ml of each excipient stock solution (filtered) was added in another 10 ml volumetric flask and volume was made up to the mark with simulated gastric fluid P^H 1.2. The samples were analyzed at 342 nm against simulated gastric fluid P^H 1.2. The results are recorded in table 6.

2.2.6 Determination of Drug Content of Solid Dispersion and Physical Mixture:

Twenty five mg of solid dispersion powder equivalent to 4.16 mg of Piroxicam was accurately weighed and transferred to a 25 ml volumetric flask. Approximately 10-15 ml of ethanol was added and flask was shaken to dissolve the content completely and the volume was made upto 25 ml. Further 1 ml of the above solution was diluted upto 10 ml with ethanol and filtered through whatman filter paper grade – 41, the filtrate was analyzed by UV spectroscopic method at 345 nm. The results are recorded in table 7.

2.2.7 Preparation of Piroxicam Fast Release Tablet Formulation

The solid dispersion of piroxicam with poloxamer-188 significantly increased the drug dissolution rate. The use of poloxamer-188 as a

carrier during preparation of solid dispersion was, thus, found to be very useful.

2.2.7.1 Preparation for Solid Dispersion:

Piroxicam and poloxamer-188 were accurately weighed in 1:4 ratio. piroxicam and the poloxamer-188 both are dissolved in a common solvent and then the solvent is evaporated under vacuum to produce a solid solution. The resulting solid dispersion of Drug : Poloxamer-188 was dried in tray dryer and packed in glass bottle.

2.2.7.2 Preparation of Piroxicam Fast Release Tablets

The solid dispersion of the piroxicam and all the excipients as mentioned in table no. 8 were weighed accurately and passed through sieve 22#. The solid dispersion, sodium starch glycolate, colloidal silicon-di-oxide, magnessium stearate were thoroughly mixed well for 10 minutes. The powder blend was then compressed into tablets using hand operated tablet compression machine.

2.2.9 In-Vitro Dissolution Rate Study of Formulated Tablets of Piroxicam - Poloxamer-188 Solid Dispersion

The dissolution rate study was performed using USP (type II) Electrolab dissolution apparatus using paddle at 50 rpm. The gastric fluid P^H 1.2 aqueous solution was used as dissolution media at temperature of 37±0.5 ^{0}C. The samples were withdrawn at suitable time intervals, diluted suitably and analyzed for drug content. Withdrawn samples were replaced with fresh dissolution media after each withdrawal. The results of dissolution study are shown in table 9 and graphically represented in fig. 3.

2.2.6 X-ray Diffraction Studies

The XRD of the drug powder was analyzed by Powder X-ray diffractometer (Bruker) having following specifications-

Power : 4 KW
Source : Cu K-α
Wavelength : 1.5418 A˚

The sample was placed on the XRD sample slide and the diffraction pattern was measured in range of $5^o<2\Theta<50°$. The X-ray diffractogram, plotted between intensity of diffracted light v/s angle of scattering (2θ value) is shown in fig 4.The powder X-ray diffraction spectra of Piroxicam, prepared solid dispersions and the physical mixtures were obtained using horizontal Rotaflex rotating anode X-ray generator instrument (bruker). The sample was spread on a graticule and pressed in such a way that sample did not fall on keeping the graticule in vertical position. The graticule was placed in sample holder and exposed to C_uK_α-radiation (40 KV, 50 MA), $2\theta = 5^o$ to 50^o at a scanning speed 3^0/min and step size 0.04^o 2θ. The X-ray diffractograms of piroxicam, physical mixture and solid dispersion so obtained are presented in fig**.** 4.1 to 4.4, respectively.

3.0 Result and Discussion:

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class used to relieve the symptoms of painful, inflammatory conditions like arthritis. Piroxicam works by preventing the production of a certain type of body chemical called prostaglandins which are involved in the mediation of pain, stiffness, tenderness and swelling.

Piroxicam is BCS class-II drug, practically insoluble in water and thus, leads to slow dissolution rate, thereby affecting the absorption from gastro-intestinal tract after oral administration. It is still a challenge for the formulation scientists to develop an oral dosage form of Piroxicam having a faster rate of dissolution.

The present research work was aimed to improve dissolution rate of Piroxicam drug. It was proposed to develop fast release formulation of Piroxicam having enhanced dissolution rate and thus, improved bioavailability.

Procured drug sample of Piroxicam was characterized by melting point determination XRD and UV spectroscopy. The melting point range of piroxicam drug sample was found to be 197-199°C., which was found identical with the

value reported in the literature. The XRD depicts presence of sharp peaks which confirmed the crystalline nature of drug sample.

During spectrophotometric analysis it was found that Piroxicam show absorbance peak (λ_{max}) at 342 nm nm, in Simulated Gastric Fluid P^H 1.2 and in ethanol peak (λ_{max}) at 345 nm. Linearity of the graph with correlation coefficient close to one confirmed that the Beer's Lambert law was obeyed in the concentration range of 5-30 µg/ml.

The selection of Carrier for Preparation of Solid Dispersion, Result of dissolution study showed that except Piroxicam : Poloxamer188 solid dispersion the drug dissolution with other solid dispersions was below 80% in 30 min. The drug release from Poloxamer 188 solid dispersions with ratio 1:4 in 30 min. was found to be maximum, i.e., 84.11%. So the poloxamer 188 was selected as a carrier for preparation of solid dispersion of Piroxicam in the further studies.

Drug-excipient compatibility study was performed under varied temperature conditions for one month. The Piroxicam was found to be compatible with the excipients selected in the present work.

The concept of formulating fast release tablet of Piroxicam using solid dispersion with Poloxamer 188 carrier was employed. The solid dispersion of piroxicam poloxamer188 was prepared by solvent evaporation technique.

The developed tablets of solid dispersion exhibited about 98% drug release in 60 min. The problem of poor dissolution of piroxicam could be successfully resolved through solid dispersion technique using poloxamer188 as a carrier.

Stability study of the developed fast release formulation of tablets was performed at accelerated temperature (40ºC) for one month. The results indicated that the developed formulation of tablet was stable for one month study period.

The X-ray diffractrogram pattern of Piroxicam showed intense and presence of sharp peaks at 10º, 16°, 24º which show that drug sample is crystalline in nature. Diffraction patterns of drug-carrier physical mixture show lesser degree of crystallinity and lesser number of characterstic peak of Piroxicam, which suggest that the crystalline nature of the drug is changed the pattern of solid dispersion was completely diffused indicating a new amorphous solid phase in solid dispersion.

4.0 Conclusion:

The solid dispersion of piroxicam with poloxamer188 significantly increased the drug dissolution rate. The solid dispersion technique using poloxamer188 as a carrier can therefore be explored to resolve the problem of poor dissolution rate and poor oral bioavailability of piroxicam.

Based on the above findings, it may be concluded that fast release formulation of piroxicam can be prepared for its dissolution rate and bioavailability enhancement. The formulation developed in the present study can be further evaluated for bioavailability enhancement.

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Table 1: Calibration Curve of Piroxicam in Ethanol at 345 nm

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.272
3	10	0.590
4	15	0.865
5	20	1.146
6	25	1.45
7	30	1.722

Table 2: Calibration Curve of Piroxicam in Simulated Gastric Fluid P^H 1.2 at 342 nm

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.231
3	10	0.429
4	15	0.672
5	20	0.881
6	25	1.096
7	30	1.338

Table 3: Selection of carrier for preparation of solid dispersion Pxm = Piroxicam, Pox = Poloxamer, PEG = Polyethylene glycol,

S. NO.	Time Min.	Cummulative % Drug Dissolved						
		Pxm: Pox407	Pxm: PEG 4000	Pxm : PVP K30	Pxm : PEG 6000	Pxm : PEG 4000	Pxm: Pox188	Physical Mixture Pxm : Pox188
Drug-Carrier ratio		1:4	1:4	1:4	1:4	1:4	1:1	1:4
1	5	11.54%	28.84%	14.91%	3.44%	27.99%	25.40%	10.39%
2	10	12.12%	32.51%	18.37%	5.1%	32.05%	31.70%	22.51%
3	15	15.45%	36.37%	25.50%	6.32%	40.19%	64.60%	24.93%
4	30	25.56%	51.50%	41.87%	15.44%	50.55%	84.11%	30.10%
5	45	42.81%	55.47%	52.00%	25.84%	55.75%	87.47%	34.97%
6	60	60.08%	58.77%	67.16%	34.48%	60.40%	89.79%	58.06%

PVP = Polyvinyl Pyrolidone,.

Table 4: Drug-Excipient Physical Compatibility Study

S. No.	Drug-excipient Blend (Drug : excipient ratio)	Initial Description	Observation of samples at different time intervals under different storage condition			
			1 Week	2 Week	3 Week	4 Week
1	piorxicam	White powder	NC	NC	NC	NC
2	piorxicam + Poloxamer 188 (1:4)	White powder	NC	NC	NC	NC
3	piorxicam + Sodium starch glycollate (5:1)	White powder	NC	NC	NC	NC
4	piorxicam + Magnesium stearate (5:1)	White powder	NC	NC	NC	NC
5	piorxicam + Colloidal silicon dioxide (5:1)	White to off white powder	NC	NC	NC	NC

*NC= No change

Table 5: Interference of Excipients in the UV Spectrophotometric Estimation of Poloxamer in Ethanol

Drug	Excipient	Drug conc. (µg/ml)	Excipient conc. (µg/ml)	Absorbance	Interference
Piroxicam	-	10	-	0.592	Nil
Piroxicam	Pox-188	10	10	0.598	Nil
Piroxicam	Mag. Stearate	10	40	0.602	Nil
Piroxicam	Colloidal silicon -di-oxide	10	40	0.573	Nil

Table 6: Interference of Excipients in the UV Spectrophotometric Estimation of Piroxicam in Simulated Gastric Fluid P^H 1.2.

Drug	Excipient	Drug conc. (µg/ml)	Excipient conc. (µg/ml)	Absorbance	Interference
Piroxicam	-	10	-	0.519	Nil
Piroxicam	Pox-188	10	10	0.522	Nil
Piroxicam	Mag. Stearate	10	40	0.525	Nil
Piroxicam	SSG	10	50	0.529	Nil
Piroxicam	Colloidal silicon -di-oxide	10	40	0.559	Nil

Pox-188 :- Poloxamer 188

Table 7: Drug Content of Piroxicam:Poloxamer188 Solid Dispersion and Physical Mixture

S. NO.	% Drug Content	
	DRUG:Poloxamer188: (1:4) Solid Dispersion	Physical Mixture
1	98.90±0.31%	96.15±0.39%
2	99.79±0.15%	96.89±0.38%
3	99.29±1.15%	97.58±0.78%

Table 8: Formulation of Fast Release Tablet of Piroxicam

S. No	Ingradient	Amount
1	Solid dispersion of piroxicam with Poloxamer 188 (1:4)	175 mg (equivalent to 35 mg piroxicam)
2	Sodium starch glycolate	16 mg
7	Colloidal silicon -di-oxide	3 mg
8	Magnesium stearate	6 mg
Total weight		200 mg

Table 9: Dissolution data of pure drug, physical mixture and developed fast dissolving tablet

S. No.	Time (min.)	% Cumulative drug dissolved		
		Pure drug	Physical mixture (Drug: Poloxamer188)	Developed fast dissolving solid dispersion tablet
1	5	3.43%	10.39%	31.50%
2	10	4.86%	22.51%	52.56%
3	15	5.23%	24.93%	65.52%
4	30	7.12%	30.10%	82.89%
5	45	7.98%	34.97%	92.55%
6	60	8.98%	58.06%	98.17%

Table 10: Stability Data of Developed Fast Release Tablets of Piroxicam

Storage conditions	Percent drug content at various time intervals		
	7 days	15 days	30 days
Room temperature (25°C)	98.60	98.47	98.11
40°C	98.56	98.33	97.81

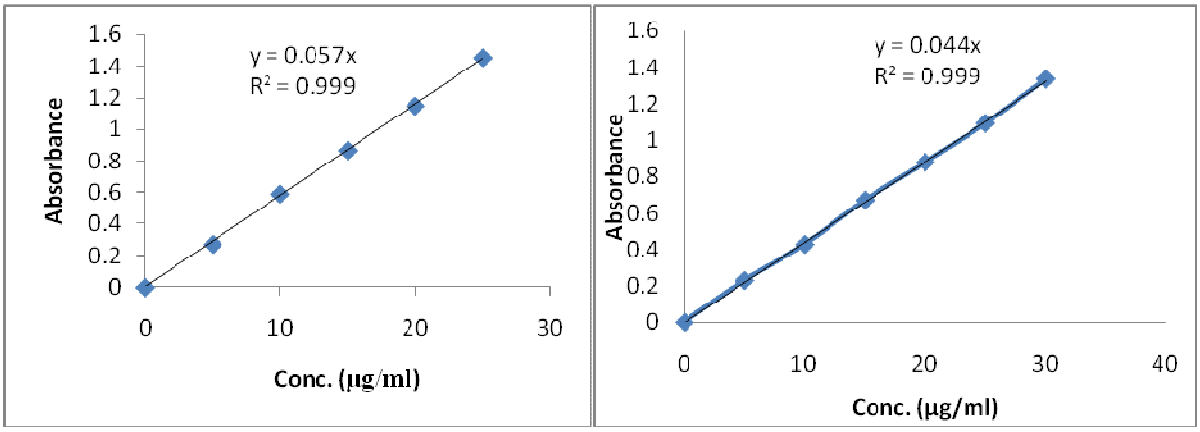

Figure1: Calibration Curve of Piroxicam in Ethanol at 345 nm and in Simulated Gastric Fluid P^H 1.2 at 342 nm

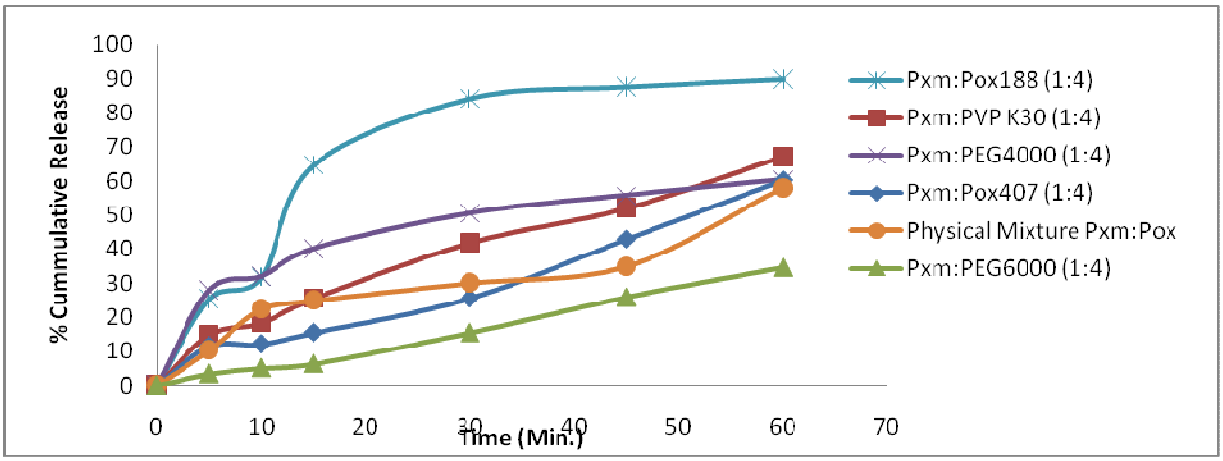

Fig. 2: Dissolution Rate of Piroxicam Solid Dispersions with Different Carriers

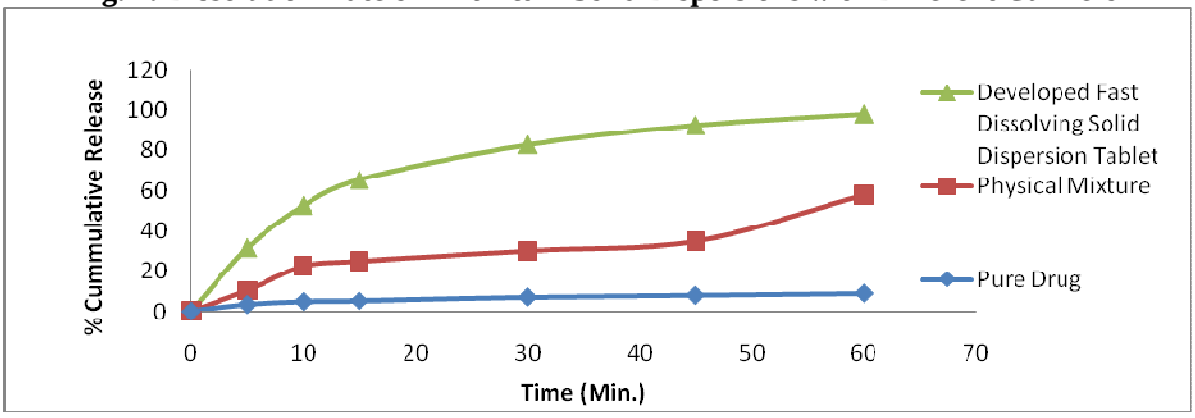

Fig. 3 Comparative dissolution profile of pure drug, physical mixture, and developed fast dissolving Tablet of solid dispersion

Figure 4: X-Ray Diffraction Studies

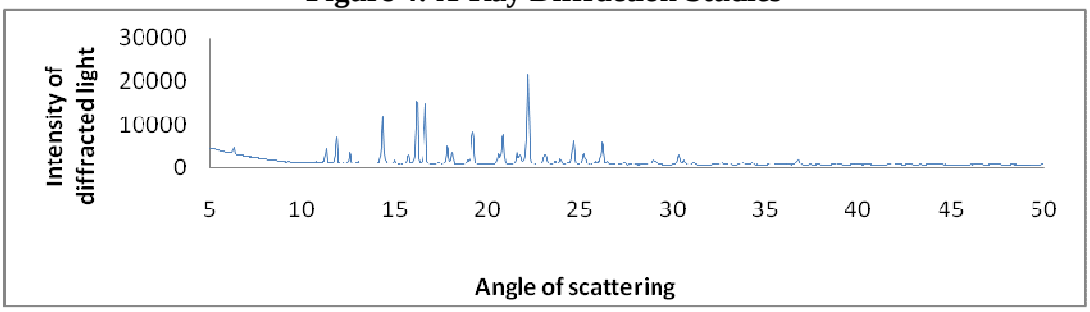

Fig. 4.1: X-ray Diffractogram of Piroxicam Drug Sample

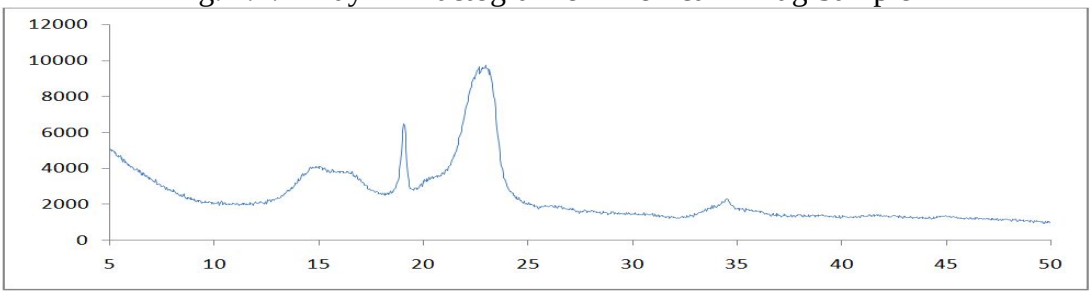

Fig. 4.2: X-RD of Ploxamer 188

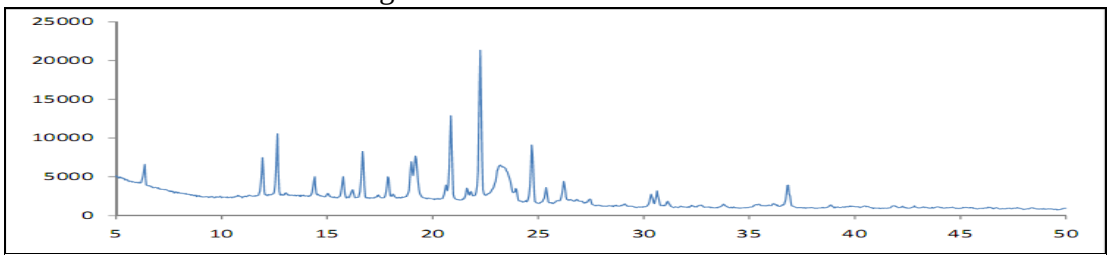

Fig. 4.3: X-RD of Physical mixture of Piroxicam : Poloxamer 188

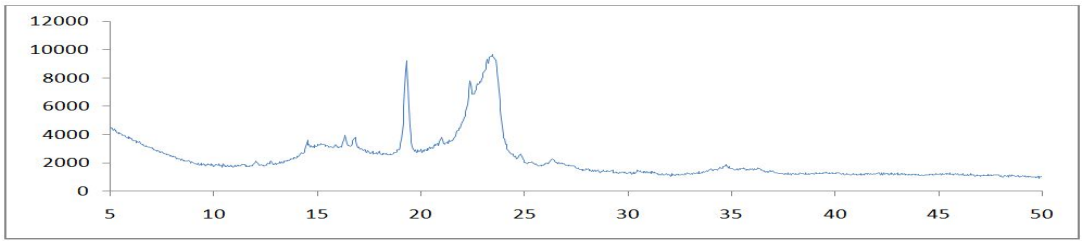

Fig. 4.4: X-RD of Piroxicam : Poloxamer188 Solid Dispersion