Research Article

Non Micronized Piroxicam-Liquid-Filled Dispersion (SEDDS) into Hard Gelatine Capsules: An Approach to Improve Dissolution and Stability of Piroxicam Formulation

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ABSTRACT

The formulation of liquid fill dispersion is an effective method of increasing the dissolution rate of poorly soluble drugs, and hence, of improving the bioavailability. The dispersion was used to prepare different dispersion of Piroxicam using triethyl citrate(TEC), acconon and polysorbate-80. The physical characteristics of the binary systems were determined Particle size analysis, Zeta potential and by HPLC. The release rate from the resulting dispersion was determined from dissolution studies by use of USP dissolution apparatus I (basket method). The dissolution rate of Piroxicam is increased in all the dispersion systems compared to that of pure drug. A liquid dispersion system of Piroxicam and triethyl citrate(TEC): acconon : polysorbate-80 blend in different ratios, was also prepared. The capsule formulation was subjected to stability studies at different temperature and humidity conditions as per ICH guidelines. Physical and chemical properties of the dispersion didn't change during a period of storage at room temperature and at 40°C, 75% RH. It was found that Piroxicam was chemically stable against the effects of temperature and humidity. However, the relative humidity and storage time exerted an effect on the dissolution behaviour of Piroxicam. The changes in dissolution behaviour after storage under conditions of high humidity and temperature might be related to the formation of Piroxicam microcrystal and to water absorption by the carrier during storage. It is predicted that acceptable shelf-lives should result when moisture resistant packaging is used for pharmaceutical formulations of this type.

Keywords: Dissolution, HPLC analysis, liquid dispersion, piroxicam (Non Micronized), stability

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INTRODUCTION

The solubility of a drug is an important factor in determining the rate and extent of absorption and thus the appearance and intensity of the therapeutic effect. Poorly soluble drugs are characterized by a low tendency to dissolve in the aqueous fluids of the administration environment. After their oral administration, this results in poor bioavailability. To overcome these problems many chemical and formulation approaches aim to improve the release rate of poorly soluble drugs. Chemical approaches are mainly based on the formation of soluble prodrugs or salts.

Formulation approaches are mainly based on the use of polymorphous (1) or amorphous (2) forms of the drug complexation, decrease of particle size and drug dispersions in soluble solid carriers. Drug dispersions are now receiving increasing attention for their easy preparation, the possibility to use a wide range of carriers, and their suitability for any drugs. An extensive review of selection of suitable carriers has been presented by Ford (3). In addition to water soluble carriers with no intrinsic solubilising properties such as high molecular weight

polyethylene glycols (PEG) and polyvinyl-pyrrolidones (PVP), the use of lipid-based amphiphilic carriers with solubilising properties.

The most widely described method of dosage form production employing such hydrophilic carriers is the liquid filling of hard gelatine capsule, where by the drug and the lipid base are heated to the molten state and filled into the capsule shell, where upon the materials are allowed to cool and solidify. There have, however, been a number of alternative approaches described in the literature, including the use of melt extrusion (Pinto & Silverio, 2001) (4), the preparation of hydrogels (Martin et al., 2002) (5), spray-congealing using ultrasound (Passerini et al., 2002) (6), and the use of super critical fluid technology to produce Gelucire coat on drug–loaded particles (Thies et al., 2003) (7).

Piroxicam is a class 2 drug with low solubility and high permeability. Its pharmacokinetic pattern is characterized by slow and gradual absorption. There are several methods for enhancing the dissolution rate of poorly water-soluble drugs including reducing particle size to increase surface area, thus increasing the dissolution rate of drug (8); solubilization in surfactant systems (9,10); formation of water-soluble complexes(11); drug derivatization such as strong electrolyte salt forms that usually have a higher dissolution rate (12); producing liquisolid formulations (13,14), manipulation of the solid state of a drug substance to improve drug dissolution i.e. by decreasing crystallinity of the drug substance through formation of solid solutions (15) and solid dispersion formulations (16,17). The most common method is to increase the surface area of the drug by micronization. But, in practice the effect of micronization is often disappointing, especially when the drugs are encapsulated or tableted (18,19). Micronised drugs also have the tendency to agglomerate as a result of their hydrophobicity, thus reducing their available surface area (20).

The aim of the present work was to prepare and characterize different dispersions of piroxicam with triethyl citrate(TEC): acconon: polysorbate-80, so as to improve its dissolution properties. In order to evaluate the effect of these carriers on piroxicam, dissolution, HPLC analysis and solubility studies were performed. Representative sample was stored at different conditions according to ICH guidelines to monitor the physical stability of the dispersion.

MATERIALS AND METHODS:

Materials:

Piroxicam was provided by Randev Chemical Pvt Ltd (Bisar Thana), Triethyl Citrate was purchased from Alfa Aesar a johnson matthey company, Acconon was obtained from Abitec and Tween -80 was purchase from Mohini Organics Pvt. Ltd (mumbai).

Solubility Study:

Solubility studies were performed according to a published method (Higuchi & Connors, 1965). An excess amount of pure Piroxicam was placed into each 20 mL test tube, to which were added 10 mL of various concentration of increasing amount of Acconon and Triethyl Citrate . The test tube were sonicated for 60min at 37°C ± 0.1 or 45°C ± 0.1(Ultrasonic bath).After 2 days, an aliquot of each mixture was trans-ferred to a 10 mL glass syringe preheated at the appro-priate temperature filtered through a Whatman filter paper(41, Ashless, circles 125mm, cat No-1441-125 GE Health care UK Limited) in ther-mostatic test tubs. About 1 mL of the clear filtrate after appropriate dilution, were allowed to stand in bath at appropriate temperature until analyzed. Concentration of Piroxicam in each aliquot was determined by using an ultraviolet spectrophotometer UV-1601(Shimadzu at 242 nm with reference to a suitable constructed standard curve. ALL Acconon and Triethyl Citrate solutions were diluted with methanol than 0.1NHCL. The apparent stability constants, Ks were calculated from the phase solubility diagrams with the assumption of 1:1 stochiometry, according to the equation

$$Ks = \frac{slope}{S\infty\ (1 - slope)} \quad (1)$$

where So is Piroxicam solubility in the absence of carrier.

Preparation of Piroxicam(Non Micronized) Dispersion:

Accurately weighed amounts of Triethyl

Citrate were placed in an glass beaker and an accurately weighed amount of Piroxicam(Non Micronized) was incorporated into the same carrier with stirring than add accurate weighted amounts of Acconon and polysorbate-80 to ensure homogeneity. The mixture was stirring until a clear homogeneous liquid was obtained, if required heat the liquid at 60°C to get clear homogeneous liquid.

Manufacture of Capsule Formulation:

The above process was followed to the point of agitation and the mixture form liquid was filled into the bodies of size 1 capsules using medicine droppers. These were then allowed to capped and then give banding. The fill weight of the capsules was 410 mg, containing 10 mg Piroxicam. The filled capsules were stored at room temperature until testing; homogeneity was indicated by the excellent clear solution of capsule. Following preparation of the dispersion, the chemical stability of Piroxicam was determined by HPLC to ensure that the drug had not undergone chemical decomposition during the preparation or in the stability. It was noted that there is no leakage or visible change in appearance was apparent during the time of storage under ambient temperature.

Dissolution Studies:

Dissolution studies were carried out in triplicate (one capsule per vessel, each contain 10mg Non micronized Piroxicam) with an Electrolab TDT-08L dissolution test (USP) in 900 mL simulated gastric fluid prepared without pepsin maintained at 37 ± 0.5°C using the basket apparatus fixed at a rotation speed of 50 rpm. Samples of 10 mL were withdrawn at various time intervals and filtered through Whatman filter paper (41, Ashless, circles 125mm, cat No-1441-125 GE Health care UK Limited) in ther-mostatic test tubs. The volume in the vessel was immediately replaced with fresh dissolution medium maintained at the same temperature. The formulations were assessed visually according to the final appearance of the emulsion formed. The corresponding concentration of Piroxicam was determined from the calibration curve made from standards of known concentration. The Concentration of Piroxicam in each aliquot was determined by using an ultraviolet spectrophotometer UV-1601(Shimadzu) at 242 nm with reference to a suitable constructed standard curve and wthout interference from Acconon, Triethyl Citrate and Tween-80. Dissolution tests were carried out for 45 min. The results presented are mean values of three determinations. Dissolution efficiency (DE) was calculated from the area under the dissolution curve at time t and expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time (Khan, 1975).

$$MDT_{in\ vitro} = \frac{\sum_{i=1}^{n} t_{mid} M}{\sum_{i=1}^{n} M} \quad (2)$$

where i is the dissolution sample number, n is the num-ber of dissolution sample times, t_{mid} is the time at the midpoint between times t_i and t_{i-1}, and M is the amount of drug dissolved between t_i and t_{i-1}.

HPLC Analysis:

Apparatus:

The analysis was performed by using the analytical balance GR-200 (AND), pH meter PHAN (Lab India), the HPLC used is 1100(Agilent). Column used in HPLC is Chromatopacl, Peerless Basic C18,250x4. 6mm,5µm, with a flow rate of 1.0 ml/min. The mobile phase consists of 600 volumes of buffer(dissolve about 6.81gm of Potassium dihydrogen Phosphate into 1000ml water, adjust pH to 3.0 with orthophosphoric acid) which are filter through 0.45µm filter and degassed in a sonicator for about 10 minutes the injection volume is 20mL and the ultra violet detection was at 230 nm.

Reagents and solutions:

Pure sample of Piroxicam (USP) and other ingredients such as Acetonitrile and water used were of HPLC and milli-Q grade. All other chemicals like Sodium Choloride, Potassium Di-hydrogen phosphate, Hydrochloric acid used were of AR grade.

Standard preparation: (11ppm)

Weight accurately about 22.0mg of Piroxicam standard in to a 100ml volumetric flask, dissolve in about 50ml diluent and dilute to volume with diluent.

Further transfer 5.0ml of above solution in to a 100ml volumetric flask and dilute to volume with the dissolution media.Filter the solution through the 0.45mm filter.

Sample preparation:

1. Switch on the dissolution apparatus and filled the 900mL of dissolution medium in each washed bowl.
2. Allow the bath liquid and medium to attain the temperature of 37±0.5°C.
3. Place six capsule separately in six bowls and start the instrument.
4. After the specified time, withdraw 10mL of the solution from a zone midway between the surface of the media and the top of the rotating basket not less than 1 cm from the vessel wall.
5. Filter the sample through 0.45mm filter.
6. Discarded the first few mL of the filtrate.

Injection Profile:

Inject blank (Dissolution Media) (1 injection) and Standard Preparation (5 injections) and check for system suitability.

System Suitability:

- The tailing factor for the Piroxicam from standard preparation should be NMT 2.0.
- The theoretical plates for the Piroxicam from standard preparation should be NLT 2000.
- RSD for the 6 replicate injections of the Piroxicam from standard preparation should be NMT 5.0.

If system suitability passes, inject sample preparation(1 injection) in to the chromatograph and the results.

Calculations and formula:

Calculate the % release of Piroxicam by the below mentioned formula :

% release of each individuals = AT/AS x WS/DS x DT/1 x P/100 x 100/LC

Where,

AT = Area response of Piroxicam in chromatogram obtained with sample preparation.

AS = Average area response of Piroxicam in chromatogram obtained with standard preparation.

WS = Weight of Piroxicam standard taken in mg

DS = Dilution of Standard preparation

DT = Dilution medium volume

P= Potency of Piroxicam Standard in % w/w on as is basis

LC= Label claim of Piroxicam in mg/ Capsule.

Stability Studies:

It was established that glycerid-based products may exhibit aging effects, whereby a range of physical properties may change on storage of the bases which are vitro, in vivo release of drug from the dosage form. Piroxicam dispersion containing 10% Piroxicam and 90% mixture of Acconon, Triethyl Citrate and Tween-80 was selected for stability on the basis of the in vitro drug release profile. The optimized formulation capsules were stored in HDPE container (packed capsules) and subjected for accelerated stability studies as per ICH guidelines i.e 25°C/60%RH and 40°C/75%RH(Grimm,1998).The desired RH was achieved by putting samples into air tight HDPE container. The container were placed inside ovens in order to control the temperature. At defined interval of time, the samples were removed from the ovens that are 1-month, 2-months, 3-months. Capsules were evaluated for the appearance, drug content and in vitro release. A simple sensitive and stability indicating HPLC method was developed and validated for content analysis during accelerated stability studies (Ficarra et al., 1991). The HPLC method was developed using chromatopack, peerless basic C18, 250x4.6mm, 5µm analytical column. The mobile phase comprising of acetonitrile: potassium dihydrogen ortho phosphate buffer [pH-3.0] in the ratio (40:60) v/v. The flow rate was maintained at 1.0ml/min and elute was monitored by using U.V detector at 230nm.The retention time of piroxicam was 12 minutes.

RESULTS AND DISCUSSION

Chemical Characterization of Piroxicam Dispersion after Preparation:

The chemical stability of Piroxicam during the fusion process was determined by HPLC assay. The assay was tested for accuracy, linearity and sensitivity. The correlation coefficients of the calibration curves (greater than = 0.998) confirm good linearity in the range of 0.5µg/ml–20 µg/ml). The area of the Piroxicam in the HPLC chromatograms of samples taken from all the final formulations accounted for greater than 97.2 of the total peak area. This

proved to be in good agreement with the theoretical values. The absence of other peaks indicates that Piroxicam didn't undergo chemical decomposition during the fusion process or appear to have interacted with the carriers.

Phase Solubility Studies:

The solubility of pure Piroxicam in water is poor, but the literature gives no exact data. In this study the solubility of Piroxicam in water was found to be about 0.0836mg/ mL. The solubility phase diagram representing the effect of increasing the concentrations of Acconon and Triethyl Citrate on the apparent solubility of Piroxicam in water at 37°C and 40°C. Comparing the two polymers, aqueous solutions of Acconon increased the solubility of Piroxicam more than that of Triethyl Citrate. Solubility experiment showed that the concentration of Piroxicam in water at 37°C, 45°C increased as a function of Acconon and Triethyl Citrate concentration. The increase in solubility was linear with respect to the weight fraction of the carrier. The shape of all solubility diagram followed an A_L-type system (Higuchi & Connors, 1965) where a linear increase of Piroxicam solubility was observed as function of Acconon and Triethyl Citrate concentrations, over the entire concentration range studied.

The increase in solubility of Piroxicam by Acconon and Triethyl Citrate may probably be explained by increased wettability of Piroxicam and micellar solubilization. Indeed, Acconon and Triethyl Citrate being surfactants cause a decrease of the interfacial tension between the drug and the dissolving solution.

Phase Solubility Study in Triethyl Citrate:

Table 1: At Room Temperature

S.NO.	Concentration	Absorbency	mg/mL after dilution	Solubility mg/mL actual
1	0.50%	0.2408	0.00680	6.80
2	0.63%	0.2896	0.00818	8.18
3	0.83%	0.4408	0.01245	12.45
4	1.25%	0.8704	0.02459	22.71
5	2.50%	1.1011	0.03110	31.10

Table 2: At 40 °C

S.NO.	Concentration	Absorbency	mg/mL after dilution	Solubility mg/mL actual
1	0.50%	0.2928	0.00827	8.27
2	0.63%	0.3388	0.00957	9.57
3	0.83%	0.4838	0.01367	13.67
4	1.25%	0.9124	0.02577	24.59
5	2.50%	1.1498	0.03248	32.48

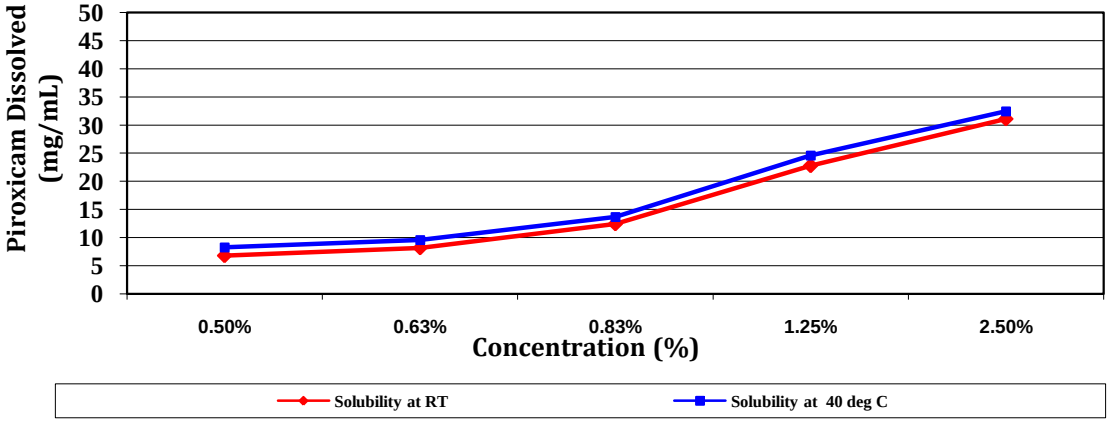

Figure 1: Phase Solubility of Piroxicam in Tri Ethyl Citrate (TEC)

Phase Solubility Study in Acconon MC8-2EP/NP:-

Table 3: At Room Temperature:

S.NO.	Concentration	Absorbency	mg/mL after dilution	Solubility mg/mL actual
1	0.50%	0.1975	0.00558	5.58
2	0.63%	0.2698	0.00762	6.86
3	0.83%	0.4225	0.01194	11.94
4	1.25%	0.4606	0.01301	13.01
5	2.50%	0.4815	0.01360	13.60

Table 4: At 40 ^{o}C

S.NO.	Concentration	Absorbency	mg/mL after dilution	Solubility mg/mL actual
1	0.50%	0.2192	0.00619	6.19
2	0.63%	0.2428	0.00686	7.62
3	0.83%	0.4726	0.01335	13.35
4	1.25%	0.5164	0.01459	14.99
5	2.50%	0.5846	0.01651	16.51

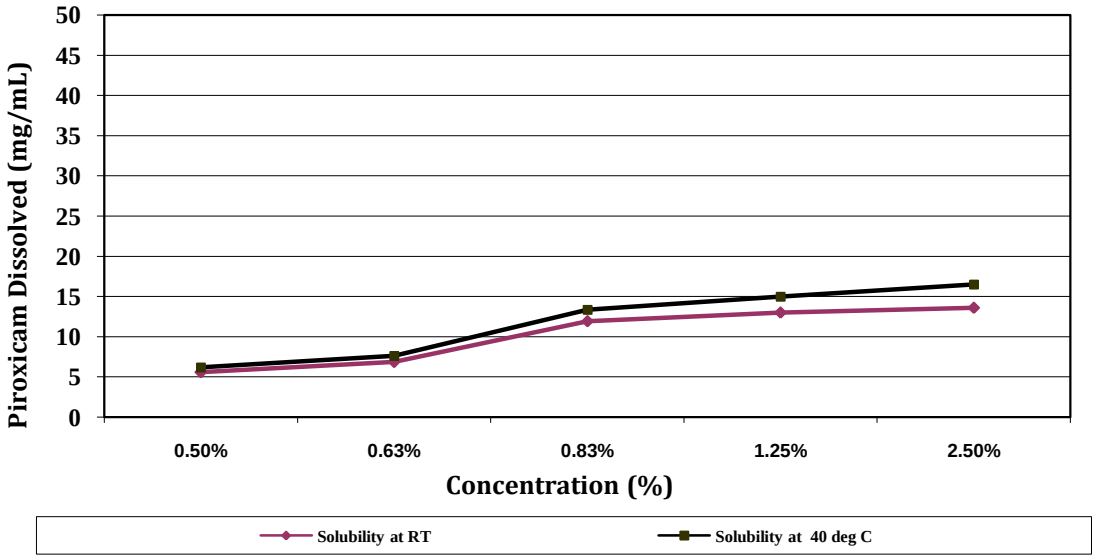

Figure 2: Phase Solubility of Piroxicam in Acconon MC8-2EP/NP

Dissolution Studies:

Triethyl citrate(TEC), Acconon and Polysorbate-80 were chosen as the hydrophilic polymers for the present studies as these highly water soluble and non-toxic polymers are known to enhance dissolution rate of insoluble drugs. Piroxicam dispersion containing a unit dose of 10mg piroxicam in a solubilizing matrix comprising either triethyl citrate(TEC), acconon and polysorbate-80 or combination thereof were prepared for in vitro evaluation. The dissolution studies were conducted in an acidic (0.1 NHCL) solution to encompass the pH values encountered in the GIT. The solubility of piroxicam in purified water is 0.086mg/mL, and this level was not achieved within 45 min. In acidic media, the dissolution of piroxicam from the powder alone was incomplete during 45 min. All the binary systems with either either triethyl citrate(TEC), acconon and polysorbate-80 displayed better dissolution properties with respect to piroxicam alone. Piroxicam being a weakly acidic drug having pKa of 5.1, all preparation showed higher concentration of dissolution in gastric fluid. The increase in solubility of piroxicam by triethyl citrate(TEC), acconon and polysorbate-80can be probably be explained by increased wettability and micellar solubilization seems more logical as both carriers being surfactants cause a decrease

in the interfacial tension between piroxicam and the dissolving solution. Similar increase in the solubility of other drugs by either triethyl citrate(TEC) has been reported (Dordunoo et al.,1991). The results of the dissolution efficiencies at 45min (DE45) and MDT of various piroxicam dispersion formulations are collected in Table 5.

All the dispersion exhibited significant faster gastric fluid dissolution rate than the pure drug. Increasing the proportion of solubilzing carrier to drug and hence the self-emulsifying efficiency of the formulation, resulted in an improvement in the drug solubilization and in the visual grading of the emulsions formed. In these studies, Triethyl citrate (TECappeared to have slightly better solubilzing properties than acconon and polysorbate-80. For example, at all ratios of piroxicam: TEC, formation of clear microemulsion in acidic medium was obtained, whereas piroxicam: Acconon formulations required higher proportion of carrier to produce similar results. In an attempt to reduce the amount of TEC incorporated into the formulation, formulations containing both acconon and polysorbate-80. The mixture of piroxicam: triethyl citrate(TEC): acconon: polysorbate-80 provided faster release than individual lipid material in dissolution media. Not less than 90% of piroxicam was released within 10 min. MDT was less than 10 min for all formulation, the dissolution efficiency after 45 min (DE45, %) were ranged from 89.7–95.4 in dissolution medium.

Table 5: Cumulative Percentage drug Release of Non Micronized Piroxicam SEDDS

S.No	Time	Cumulative Percentage drug Release of Piroxicam SEDDS Formulation					
		A	B	C	D	E	F
1	05	5.20	22.61	6.25	9.34	12.26	83.13
2	10	5.47	28.62	11.80	18.11	29.69	88.53
3	15	6.72	38.07	19.56	24.83	49.43	92.46
4	30	11.30	52.78	50.49	70.32	67.69	96.13
5	45	12.54	63.32	59.97	77.12	80.66	100.17

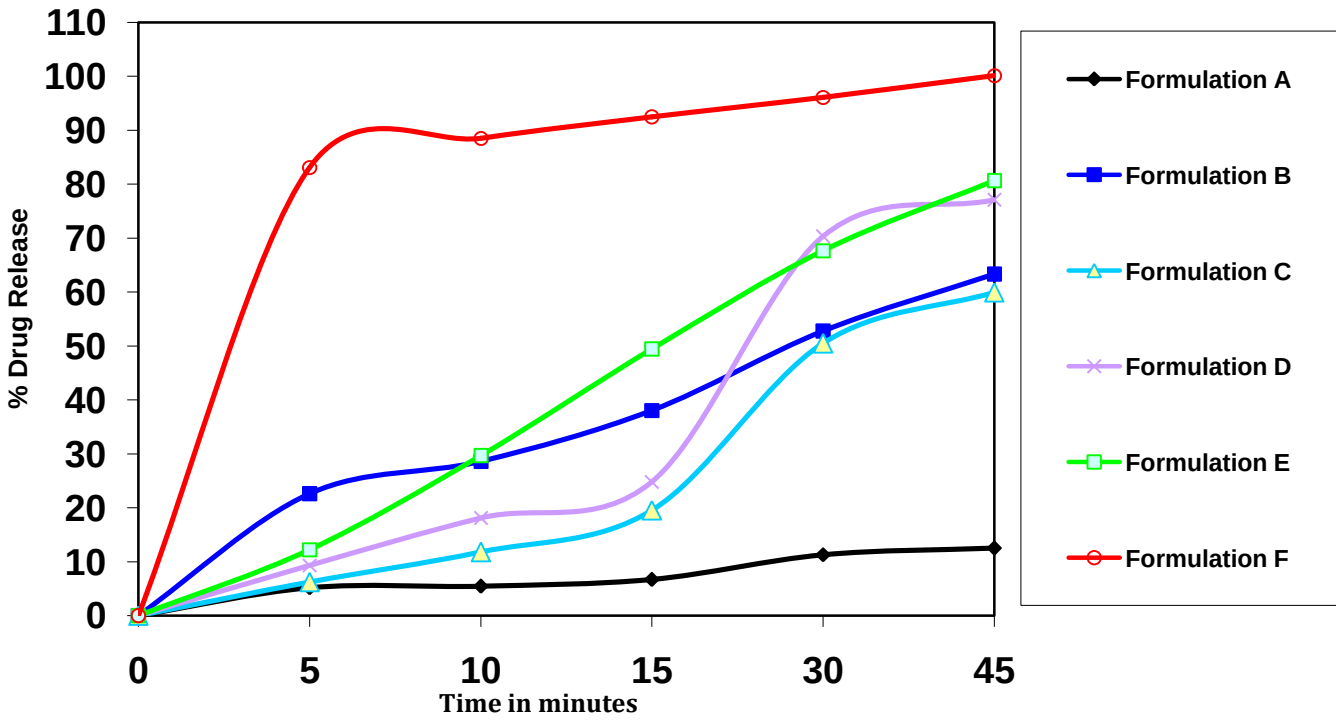

Figure 3: Cumulative Percentage drug Release of Non Micronized Piroxicam SEDDS 10mg in 0.1N HCL

HPLC ANALYSIS:

The self emulsifying drug delivery system (SEDDS) formulation of Piroxicam is a novel and versatile approach for overcoming the formulation difficulties of drugs with poor aqueous solubility. The present developed method is novel for the determination of Piroxicam in SEDDS formulations. The method was found to be specific as excipients in the formulation did not interfere in the estimation of piroxicam in SEDDS formulation.

Piroxicam standard having concentration 50mg/ml was scanned in UV- region between 200-400 nm. λ max of Piroxicam was found to be at 230 nm. The Piroxicam peak in the sample was identified by comparing with the Piroxicam standard and the retention time was found to be around 12 minutes.. The estimation Piroxicam was carried out by RP-HPLC using Mobile phase having a composition volumes of phosphate buffer, 40 volumes of Acetonitrile and 60 volumes of buffer (40 : 60 v/v). The ratio pH was found to be 3.0. Then finally filtered using 0.45µ nylon membrane filter and degassed in sonicator for 10 minutes. The column used was C18 Inertsil ODS 3V (150 mm x 4.6 mm x 5 µ particle size). Flow rate of Mobile phase was 0.8 ml/min, System suitability parameters such as the tailing factor for the Piroxicam from standard preparation should be NMT 2.0, the theoretical plates for the Piroxicam from standard preparation should be NLT 2000, RSD for the 6 replicate injections of the Piroxicam from standard preparation should be NMT 5.0.

The results of analysis showed that the amount of drug was in good agreement with label claim of developed SEDDS formulation. It was observed that there were no marked changes in chromatogram, The results indicated that the developed formulation was stable up to 12-14 hours which was sufficient for completing the analytical procedures. The developed method was specific and reproducible for the quantitative determination of piroxicam in SEDDS formulation with a good resolution and high sensitivity.

The Accuracy limit is the % recovery should be in the range of 98.0% to 99.8%. The developed method shows that the accuracy is well within the limit, which shows that the method is capable of showing good accuracy.

Optimized chromatographic conditions:

Table 6: Optimized chromatographic conditions

Parameter	Optimized condition
Chromatograph	HPLC Agilent-1100
Column used	Chromatopack, Peerless Basic C18, 250 x 4.6mm, 5mm
Wavelength	230nm
Flow rate	1.0ml/min
Injection volume	20ml
Mobile Phase	Acetonitrile and Buffer (40:60)
Column Temperature	40°C

System suitability parameters:

Table 7: System suitability parameters

Parameter	Piroxicam
Calibration rang (µg/ml)	5-150
Theoretical plates	NLT 2000
Tailing factor	NMT 2.0
% Recovery	98.0% - 99.8%

Product Name :-	PIROXICAM CAPSULES	Batch No.:-	
Sample Name :-	BLANK	A.R.No. :-	
Sample No. :-	2	Test :-	RELATED SUBSTANCES
Sample Type :-	unknown	Stage :-	
Program File :-	PIR_CAP_REL_1	Pack Details :-	1
Method File :-	PIR_CAP_REL_1	Vial Number :-	51
Date Acquired :-	24.11.2012 16:20:38	Injection Volume :-	20.0 µl
Qnt Last Update :-	18.12.2012 12:42:10	Wavelength :-	230 nm
Instrument ID :-	1080-HPLC-0008	Run Time :-	60.00 mins
Column No. :-		Analyst :-	rukmani v
Sequence Name :-	PIR_REL_1_1080-MS-1200527_2411		
Sequence Path :-	STAR\PIROXICAM CAPSULES\SEQUENCES\2012\PIR_REL_1_1080-MS-1200527_2411.SEQ		
Parameters :-	1		

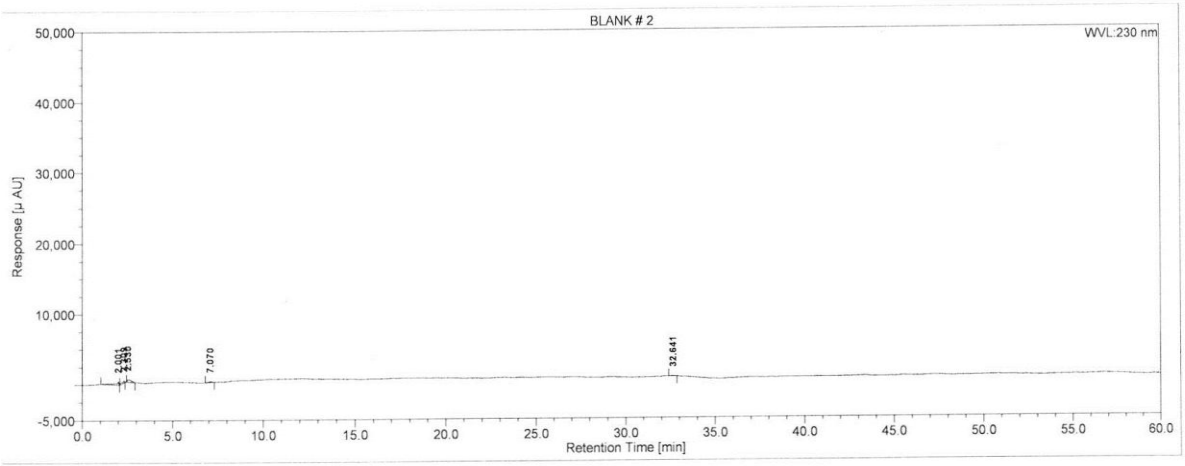

Figure 4: Chromatograph Representing the Blank

Product Name :-	PIROXICAM CAPSULES	Batch No.:-	
Sample Name :-	STANDARD	A.R.No. :-	
Sample No. :-	3	Test :-	RELATED SUBSTA
Sample Type :-	standard	Stage :-	
Program File :-	PIR_CAP_REL_2	Pack Details :-	1
Method File :-	PIR_CAP_REL_2	Vial Number :-	52
Date Acquired :-	24.11.2012 17:22:13	Injection Volume :-	20.0 µl
Qnt Last Update :-	18.12.2012 08:50:03	Wavelength :-	230 nm
Instrument ID :-	1080-HPLC-0008	Run Time :-	15.00 mins
Column No. :-		Analyst :-	rukmani v
Sequence Name :-	PIR_REL_1_1080-MS-1200527_2411		
Sequence Path :-	STAR\PIROXICAM CAPSULES\SEQUENCES\2012\PIR_REL_1_1080-MS-1200527_2411.SEQ		
Parameters :-	1		

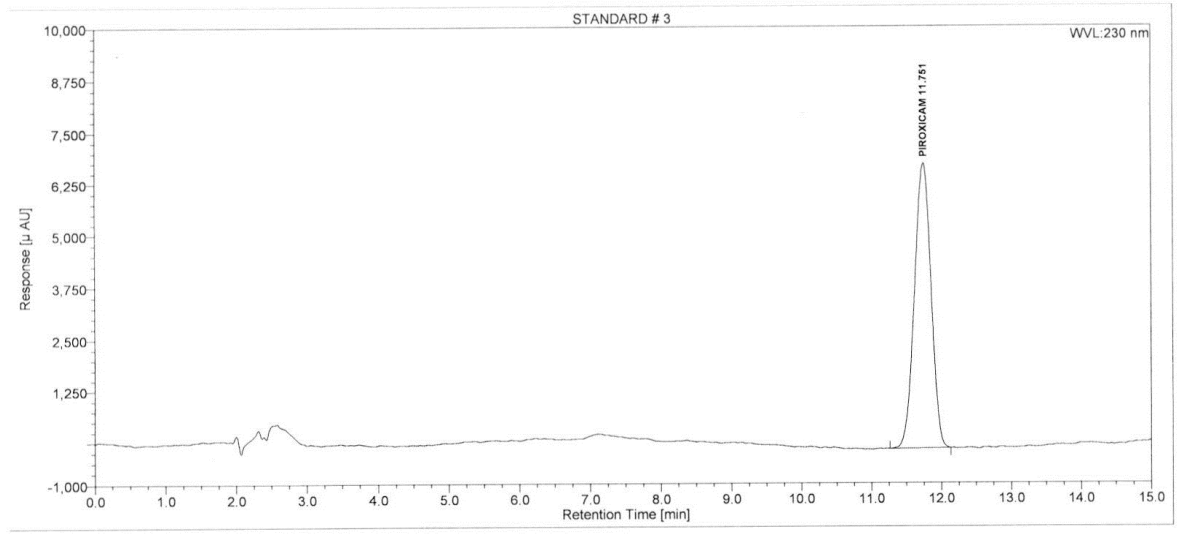

Figure 5: Chromatograph Representing the Standard

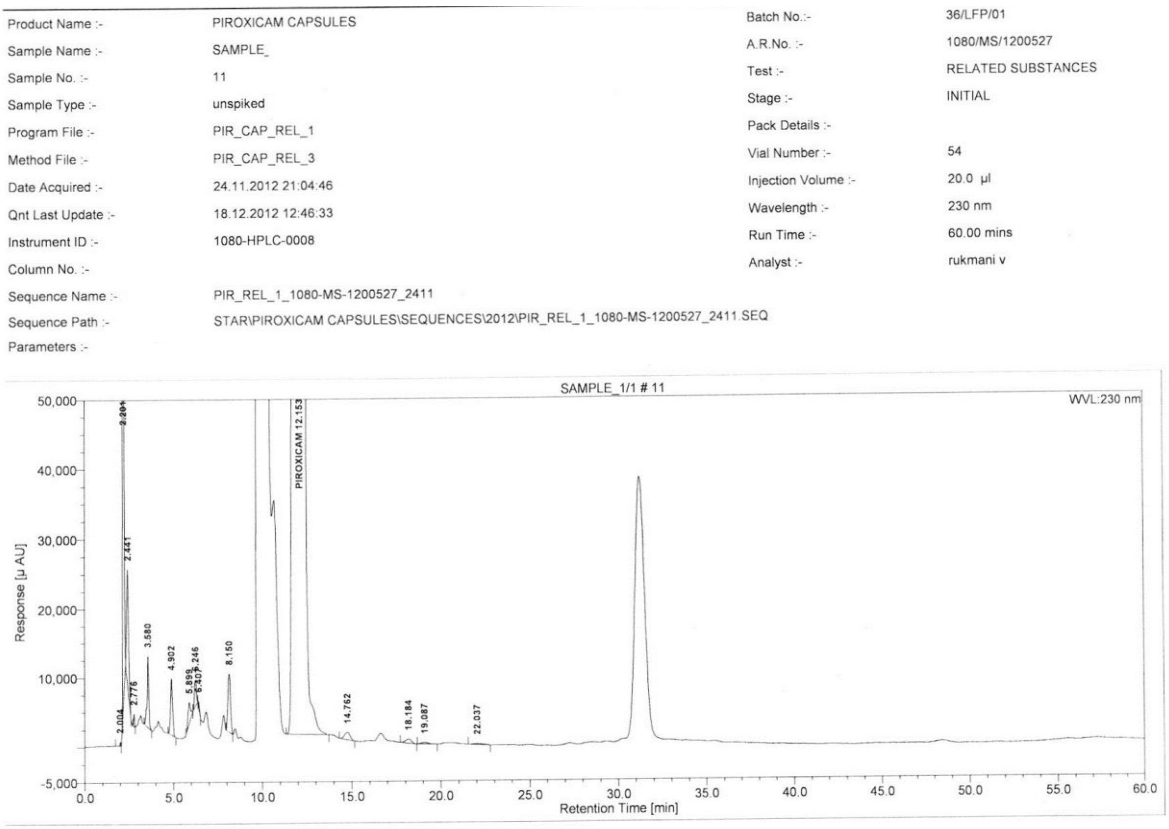

Figure 6: Chromatograph Representing the Sample

Stability Studies:

For the stability study, one of the dispersion (piroxicam with triethyl citrate(TEC): acconon: polysorbate-80,) was investigated after storage for 1, 2, and 3 months under different conditions. In freshly prepared formulation, piroxicam is present in the non micronized form and the DSC patterns display no peaks that can be attributed to piroxicam crystals either before or after storage at room temperature or at 40°C/75% RH, suggesting that crystallization doesn't occur in this case. No new peaks, no change in the thermogram of the dispersion after storage under these conditions indicating that neither the drug nor the matrix system underwent any phase change. Also, chemical stability of the active ingredient improved to be unchanged upon aging of the capsule formulation during the period of the study which is confirmed by HPLC assay.

It was concluded that lipid excipients composed of triglycerides can undergo polymorphic transitions, precipitation or crystallization with time, accompanied by corresponding changes in their properties and in rate of release of the formulated active principles (Laine et al., 1988). Amorphous to crystalline conversions are observed, the kinetics of which are found to be both temperature and relative-humidity dependent.

Since it is generally assumed that there is some kind of correlation between the dissolution curve of immediate release dosage forms obtained in an in vitro study and the oral absorption/bioavailability in an in vivo situation. This would imply that a range of the dissolution properties of the dispersions upon storage can potentially lead to a reduced uptake of the drug from the gastrointestinal tract. Hence, when developing a drug-dispersion system one should perform a stability study to elucidate which conditions result in no or only a minor decrease of its physical structure in order to stay within the limits of the specification for the dissolution of the dosage form. In this case, storage at conditions of low humidity might be adequate to store such formulation.

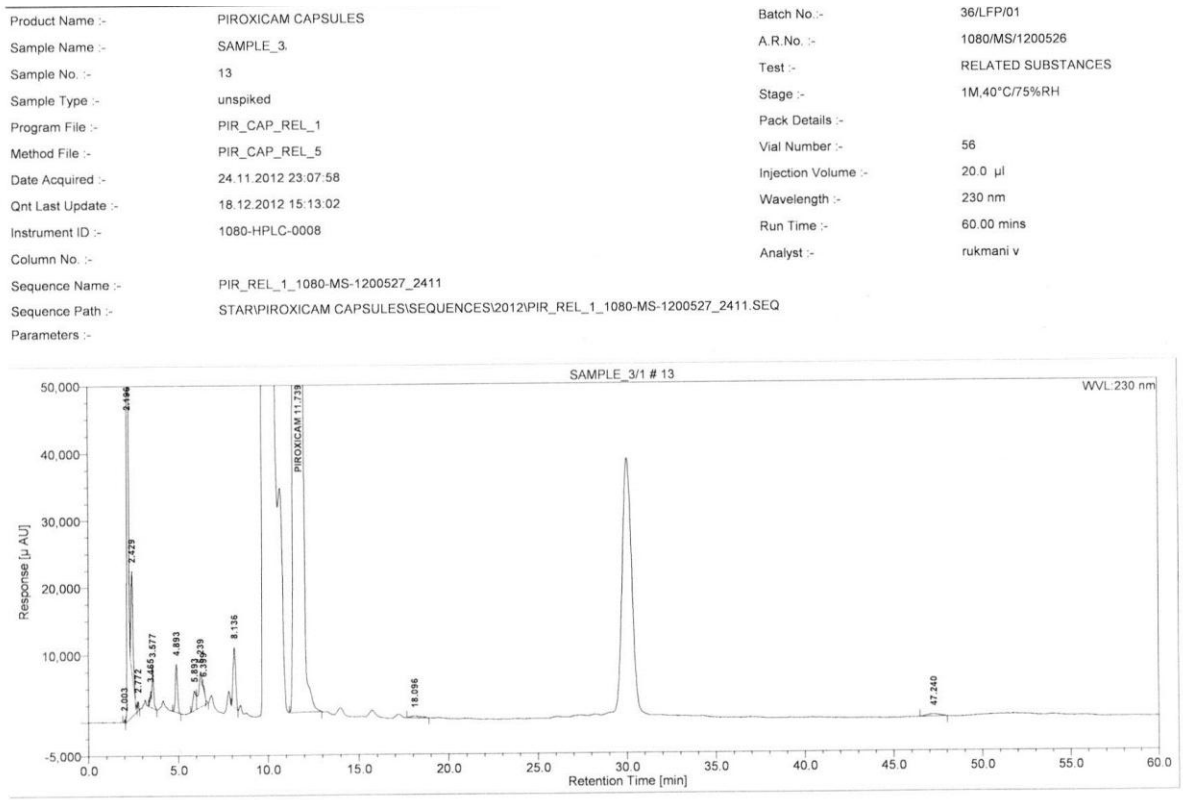

Figure 7: Chromatograph Representing the 3-Months Stability Sample

CONCLUSION

The present results of investigation show the suitability of triethyl citrate(TEC): acconon: polysorbate-80 as the carrier for preparation of piroxicam dispersion filled into hard gelatine capsules. As mentioned above, these substances are widely used as pharmaceutical excipients. The dissolution rates of piroxicam dispersions were higher than that of pure drug; this was possibly caused by the increase in drug wettability.

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