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ENHANCEMENT OF SOLUBILITY OF ACECLOFENAC BY RECRYSTALLIZATION METHOD USING POLAR SOLVENTS

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ABSTRACT

Aceclofenac crystals were prepared by Recrystallization from selected solvents such as ethanol and methanol under different working conditions and using different additives like HPMC, PVP, PEG 4000 Sodium CMC, Chitosan, Gelatin, and Sodium Alginate. Obtained crystals were characterized by photomicrography, scanning electron microscopy, X-ray powder diffractometry, FT-IR spectrometry, differential scanning calorimetery, thermogravimetric analysis and Karl Fischer titration. The crystals were evaluated for melting point, LOD, particle size, solubility and dissolution. It was found that the newly developed crystals were different from each other with respect to physical properties, but they are chemically identical. The crystals obtained from ethanol produced prismatic and rod shaped and that obtained from methanol produced hexagonal and thin pole shaped crystals. But the crystals obtained with alcoholic (ethanolic / methanolic) solution of drug in the presence of produced smooth needle shaped crystals. X-ray diffraction spectra of pure drug and prepared crystals indicate that existence of four distinct crystal modifications of orthorhombic for pure drug, triclinic, monoclinic and hexagonal when modified with different solvents, methods and additives. Hence, both X-ray diffraction spectra and differential scanning calorimeter study of the newly developed crystals, clearly indicate that Aceclofenac exist in different crystal modifications. The solubility of newly developed crystals was about 1.5 to 1.9 times higher in distilled water than that of untreated Aceclofenac. The flow properties as angle of repose, car's compressibility index and Hausner's ratio suggested that there was slight variation for obtained crystals due to change in crystal shape and particle size.

KEYWORDS: Aceclofenac; Recrystallization; Crystal shape; Solubility; *Invitro* dissolution

INTRODUCTION

Recently in the field of pharmaceutical technology, great efforts are being directed towards the prefabrication of existing drug molecules in the way of solving problems related to poor water solubility, bioavailability flow ability, compressibility, dosing problem, stability and toxicity.[1]

Crystals can be modified by recrystallizing the drug in different ways, which affect physical and physicochemical properties such as melting point, solubility, true density, dissolution profile, flow ability and tablet ability. Recrystallization method is simple and inexpensive enough for scaling up to commercial level. It reduces time and cost by enabling faster operation, less machinery and fewer personnel. It gives important advances in the different pharmaceutical dosage form technology.[1]

The vast majority of active pharmaceutical ingredients (APIs) are formulated as solid dosage forms due to their convenience and excellent patient compliance, with most marked products containing API(s) and/or excipients in the crystalline state state. The bioavailability of a solid dosage form is strongly dependant on physical properties of the actual API to be formulated (crystalline form, morphology, particle size distribution).[1]

Crystallization[2, 3, 4, 5]

A crystal may be defined as a homogenous particle of solid which is formed by solidification under favorable conditions, of a chemical element or a compound, arranged at definite angles to one another in definite geometric form. In other words, a crystal is one in which the internal atomic or molecular arrangement is regular and periodic in three dimensions over intervals which are large compared with unit of periodicity. The smallest arrangement of atoms and molecules which repeats regularly and is a true representation of crystal structure is known as ‘Unit Cell’.

Crystallization is complex unit operation widely used in the industry for the production of pure solid substances. Many drugs exist in the crystalline solid state due to reasons of stability and ease of handling during the various stages of development. Recent advances in crystallization technology have made it possible to use it as a particle design technique to

change the micromeritic properties, compressibility and Wettability of pharmaceutical substances.

Crystallization differs from precipitation in that the product is deposited from a supersaturated solution. Precipitation occurs when solutions of materials react chemically to form a product, which is sparingly soluble in the liquid and therefore deposits out. Precipitates are insoluble substances produced by a chemical reaction, therefore it is irreversible process. But the products of crystallization can be redissolved if the original conditions of temperature and solution concentrations are restored.

Crystal forms[2, 4]

In a crystal there is a repetitive arrangement of constituent atoms in a three-dimensional network. There are only finite numbers of symmetrical arrangements possible for a crystal lattice, and these may be termed as crystal forms. It is described by relationship among the crystal axes and angles between them. The various types of crystal forms are given in following figure.

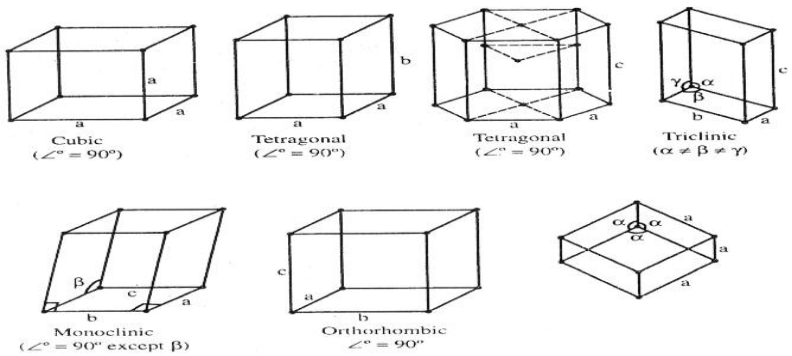

Fig. 1: Crystal forms

MATERIALS AND METHOD

Table 1: Materials and sources

Sr.No.	Materials	Source
1.	Aceclofenac	Amoli Organics Pvt Ltd, Vapi (Gujarat).
2.	Ethyl alcohol AR 99.9%	Changshu Yangyuan Chemical
3.	Methanol AR	Ranbaxy Fine Chem. Ltd, New Delhi
4.	Hydroxypropylmethyl cellulose	Loba Chemie Pvt Ltd, Mumbai.
5.	Polyvinyl pyrrolidone	Loba Chemie Pvt Ltd, Mumbai.
6.	Polyethylene glycol 4000 LR	SD Fine Chem Ltd., Mumbai
7.	Potassium dihydrogen orthophosphate	SD Fine Chem Ltd., Mumbai
8.	Sodium hydroxide LR	SD Fine Chem Ltd., Mumbai
9.	Carboxymethyl cellulose sodium	Loba Chemie Pvt Ltd, Mumbai.

10.	Chitosan	SD Fine Chem Ltd., Mumbai
11.	Gelatin	SD Fine Chem Ltd., Mumbai
12.	Sodium alginate	Loba Chemie Pvt Ltd, Mumbai.

Construction of calibration curve:

Standard Calibration Curve of Aceclofenac[6, 7]

Standard Solution:

100 mg of Aceclofenac was dissolved in 100 ml ethanol, methanol and phosphate buffer pH 7.4 to get a concentration of 1 mg/ ml (1000 µg/ml) in respective solvents.

Working standard Solution

From standard solution, 10 ml of solution were taken and dissolved in 100 ml of respective solvent and from this 1ml, 2ml, 3ml, 4ml, 5ml solution were taken and dissolved in 25 ml to produce the 4, 8, 12, 16, 20 µg/ml concentrations respectively. The absorbance of prepared solutions of Aceclofenac was measured at 275 nm in Shimadzu UV/visible 1700 spectrophotometer against respective solvent as blank. The absorbance data for standard calibration curve are given in Table No. 2, 3, 4 and plotted graphically as shown in the Fig. No-2, 3, 4.

Selection of solvents for crystallization on the basis of solubility studies in organic solvent[8, 9]

An excess quantity of Aceclofenac (pure drug) was taken in 10ml of different solvents in a shaking water bath (100agitations/min) for 24 hr at room temperature. The solution was then passed through a Whatman (No.1) filter and the amount of drug dissolved was analyzed spectrophotometrically (UV-1700, Shimadzu, Tokyo, Japan) after suitable dilutions.

Methods of preparation of Aceclofenac crystals[10, 11]

Two solvents ethanol and methanol were selected based on their solubility used to study the effect of solvent on the crystal growth.

a) Ethanol solutions were prepared by dissolving 1.150gm of Aceclofenac in 10ml ethanol at 65^0C to form a clear solution.
b) Methanol solutions were prepared by dissolving 1.150gm of Aceclofenac in 10ml ethanol at 55^0C to form a clear solution.

In order to investigate the effect of cooling rate the following methods were used to crystallize Aceclofenac from the both ethanol and methanol solutions.

Method I: Rapid Cooling

The solution was immediately transferred to freezer (-10^{0}C) and left for period of 48 hours.

Method II: Cooling to Room Temperature then Fridge

The solution was left to reach room temperature 25^{0}C (cooling rate of 1.5± 0.3^{0}C) and then transferred to fridge (6-8^{0}C) and was left for a period of 48 hours. The precipitated crystals from the above two methods were collected by filtration through a sintered glass funnel vacuum.

Method III: Evaporation to Room Temperature

The solution was left at room temperature until the solvent was completely evaporated.

Method IV: Watering Out technique

The solution (55-60^{0}C) was rapidly added to 20ml cold water (10^{0}C) and under agitation by means of a glass rod and then left for 2 days at 10-15^{0}C. The crystals were collected by filtration using a sintered glass funnel vacuum.

Methods of preparation of Aceclofenac crystals using different additives[10, 11]

To study the effect of additives on the crystallization of Aceclofenac Method IV i.e. Watering Out technique was modified by replacing cold water to 0.25%w/v aqueous solutions of additives i.e. Hydroxypropyl methylcellulose, Polyvinyl pyrollidon, Polyethylene glycol 4000, Carboxymethylcellulose sodium, Chitosan, Gelatin and Sodium alginate.

Characterization of prepared Aceclofenac crystals[12-16]

1) Photomicrography

Photomicrographs of Aceclofenac crystals were obtained under Stereo zoom Microscope with CCD camera attachment (Model S8APO, Leica, Germany).

2) Scanning electron microscopy

Dry crystals were placed on an electron microscope brass stub coated with gold in an ion sputter. The picture of crystals was taken by random scanning of the stub. The SEM analysis of the crystal was carried out by using JEOL-6360A analytical scanning electron microscope.

3) Powder X-Ray Diffractometry (PXRD)

The x-ray diffraction patterns of pure drug and the optimized formulations were recorded using Philips analytical XRD B.V. (Model PW 3710) with chromium target.

4) Differential Scanning Calorimetry (DSC)

DSC was performed using SDT 2960 (Simultaneous DSC-TGA), (TA instruments Inc. USA) calorimeter to study the thermal behavior of drug alone, prepared crystal using solvents, mixture of drug and polymer or prepared co-crystals.

5) Thermal Gravimetric Analysis (TGA)

TGA was conducted at heating rate of 5^0C/min using SDT 2960 (Simultaneous DSC-TGA), TA instruments Inc., USA.

6) Infrared (IR) Spectroscopy

IR spectroscopy was conducted using a Shimadzu FT-IR 8400 spectrophotometer (Shimadzu) and spectrum was recorded in the wavelength region of 4000-400cm^{-1}.

7) Karl-Fischer (Kf) Aquametry

Karl- Fischer titrimeter (Aqua Cal) was used for the determination of water content.

8) Determination of Loss On Drying

Loss on drying of prepared Aceclofenac crystals was determined on 1.000gm by drying in an oven at 100-105^0C until the weight of crystals remains constant.

9) Particle size

Measurement of the particle size distribution and mean diameter of beads were carried out with an optical microscope. Stage micrometer was used to calculate calibration factor. The particle size was calculated by multiplying the number of division of the ocular disc occupied by the particle with calibration factor. Fifty randomly chosen crystals were taken to measure their individual shape and size.

10) Solubility studies of prepared Aceclofenac crystals in distilled water

An excess amount of prepared Aceclofenac crystals were taken in 10ml of distilled water in a shaking water bath (100agitations/min) for 24 hr at room temperature. The solution was then passed through a Whatman (No.1) filter and the amount of the drug dissolved was analyzed spectrophotometrically (UV-1700, Shimadzu, Japan) after suitable dilutions.

11) Dissolution study of prepared crystals[15-17]

The *in vitro* release of drug from pure drug and prepared crystals were carried out for 3 hours using paddle type Electrolab Tablet Dissolution Apparatus USP XXIII containing 900 ml of dissolution medium maintained at 37±0.5ºC and speed of agitation at 100 rpm.

An accurately weighed crystals equivalent to 50 mg of Aceclofenac as added into each dissolution flask. At prefixed time (every 15 minutes), 5 ml of samples were withdrawn and assayed spectrophotometrically for the drug content at 275 nm using Shimadzu-1700 UV-Visible spectrophotometer after suitable dilutions. The mean of three determinations was used to calculate the drug release from each of the formulation.

RESULTS

Table 2: Calibration curve of Aceclofenac in ethanol, methanol & pH 7.4 phosphate buffer solution

Concentration (mcg/ml)	Abs in Ethanol	Abs in Methanol	pH 7.4 phosphate buffer
0	0.00±0.00	0.00±0.00	0.00±0.00
4	0.161±0.005	0.151±0.004	0.109±0.005
8	0.313±0.001	0.271±0.007	0.210±0.008
12	0.456±0.006	0.417±0.003	0.320±0.004
16	0.607±0.003	0.544±0.004	0.426±0.007
20	0.769±0.002	0.699±0.002	0.526±0.005

*Average of three determinations

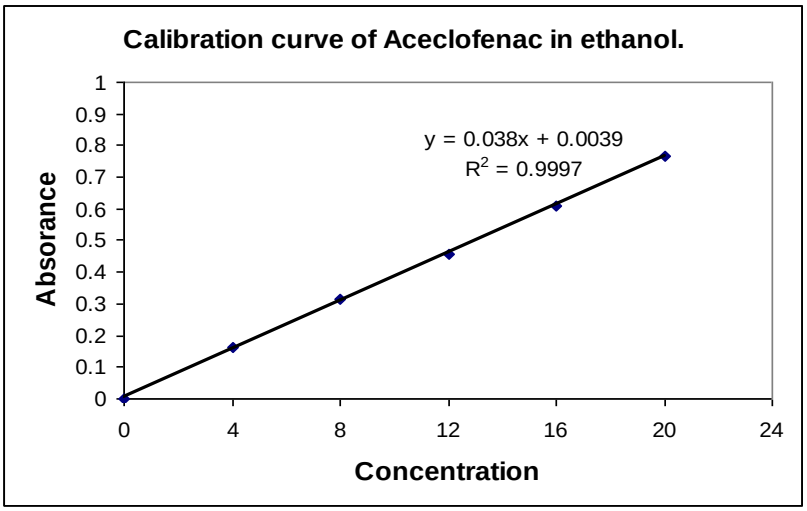

Fig. 2: Calibration curve of Aceclofenac in ethanol solution

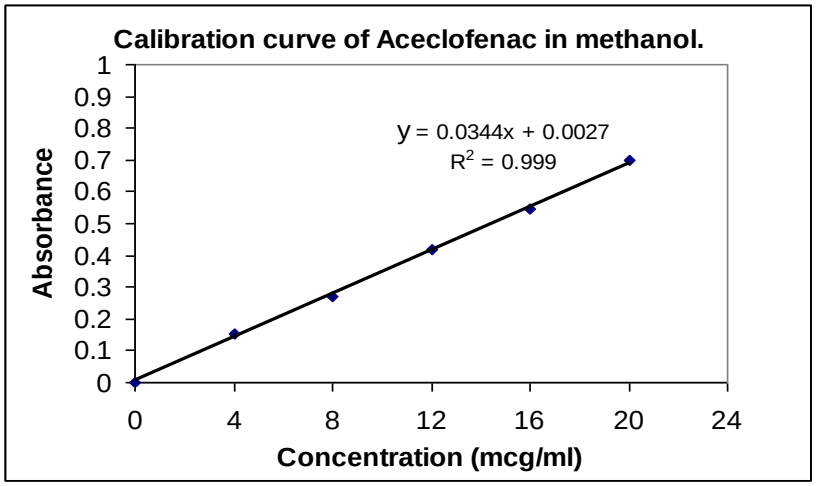

Fig. 3: Calibration curve of Aceclofenac in methanol solution

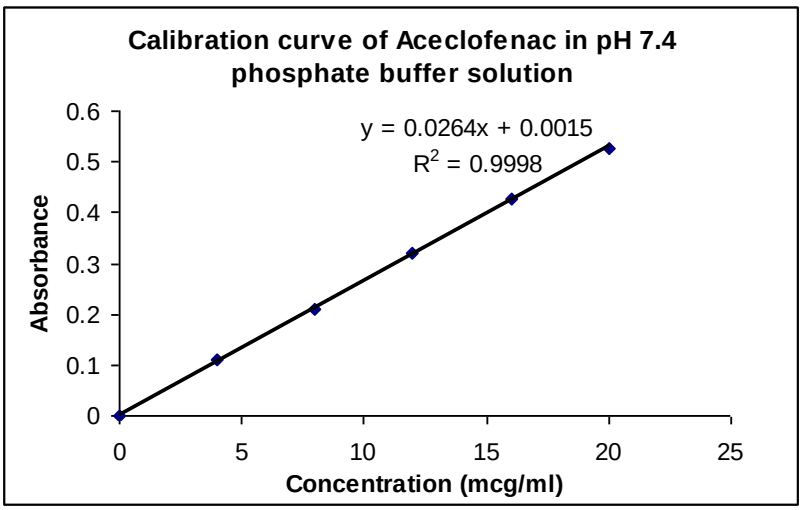

Fig. 4: Calibration curve of Aceclofenac in pH 7.4 phosphate buffer solution

Table 3: Selection of solvents for crystallization on the basis of solubility studies in organic solvents

Sr. No.	Solvent	Type of solvent	Solubility (mg/ml)± SD	As per I.P. limit
1.	Ethanol*	Polar protic	113.48± 0.328	Soluble
2.	Methanol*	Polar protic	110.79± 0.359	Soluble
3.	Dichloromethane	Nonpolar	4.276± 0.043	Slightly soluble
4.	Propyl alcohol	Polar protic	36.64± 0.174	Soluble
5.	Diethyl ether	Nonpolar	3.32± 0.039	Slightly soluble
6.	Chloroform	Nonpolar	65.658± 0.237	Soluble
7.	Benzene	Nonpolar	49.01± 0.231	Soluble
8.	Cyclohexane	Nonpolar	2.375± 0.011	Slightly soluble
9.	Acetonitrile	Dipolar aprotic	112.66± 0.284	Soluble
10.	Distilled water	Polar protic	0.0855± 0.002	Practically insoluble

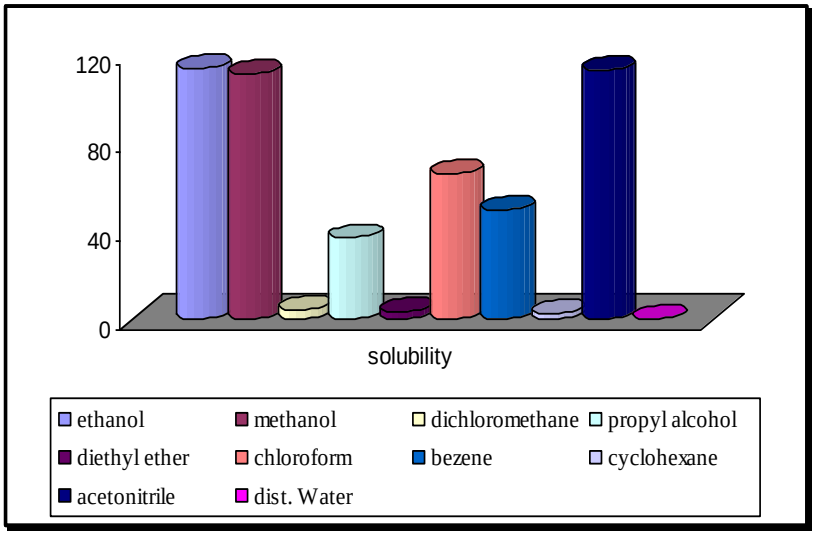

Fig. 5: Solubility studies of Aceclofenac in organic solvents

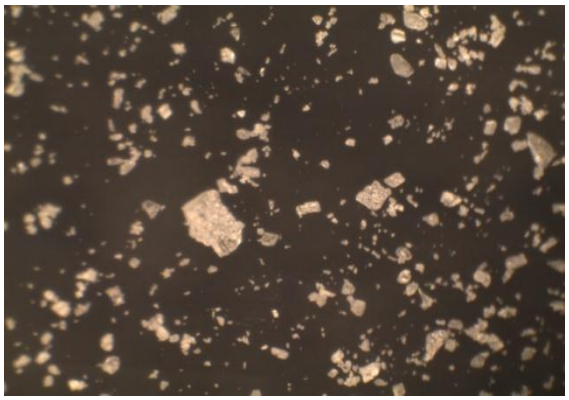

Fig.6: Photomicrograph of Pure *Drug*

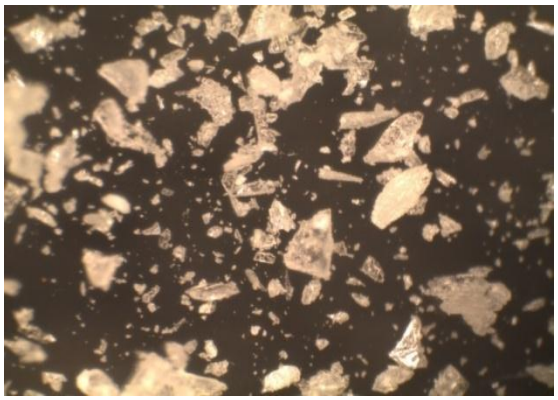

Fig. 7: Photomicrograph of AE1

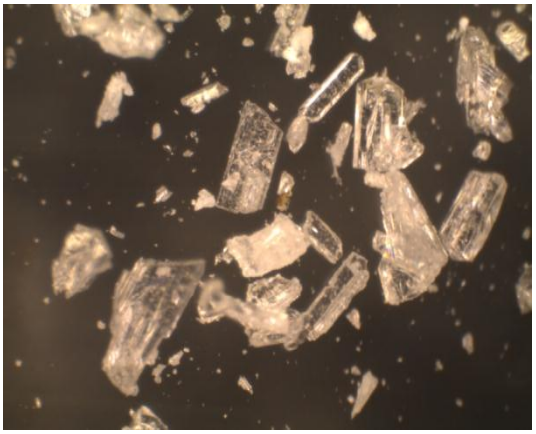

Fig. 8: Photomicrograph of AE2

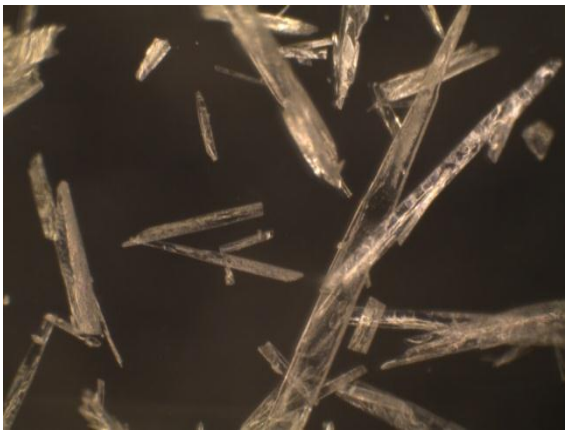

Fig. 9: Photomicrograph of AE4

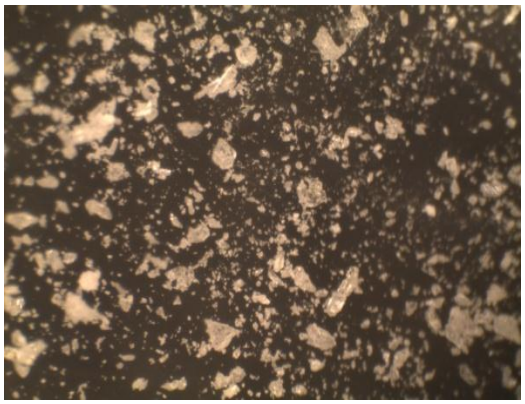

Fig. 10: Photomicrograph of AM1

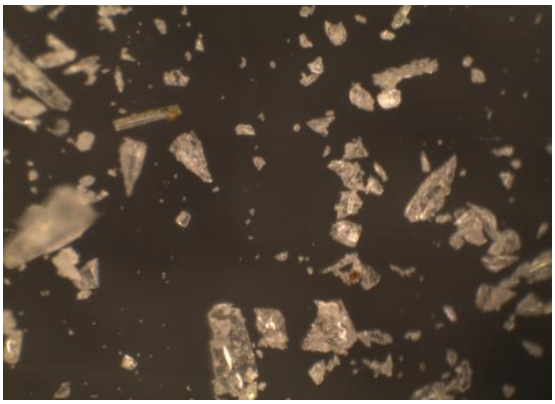

Fig. 11: Photomicrograph of AM

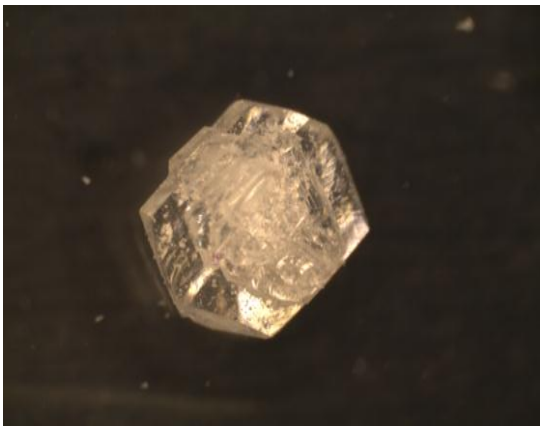

Fig. 12: Photomicrograph of AM3

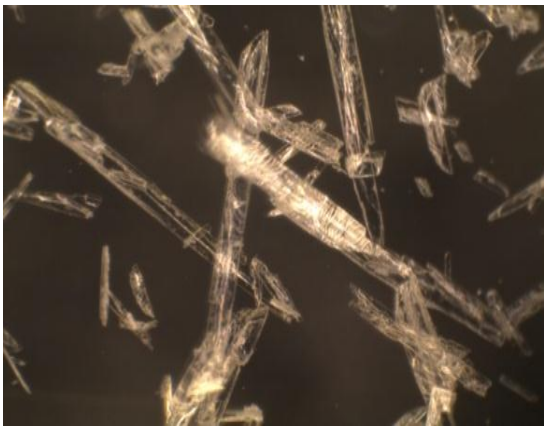

Fig.13: Photomicrograph of AM4

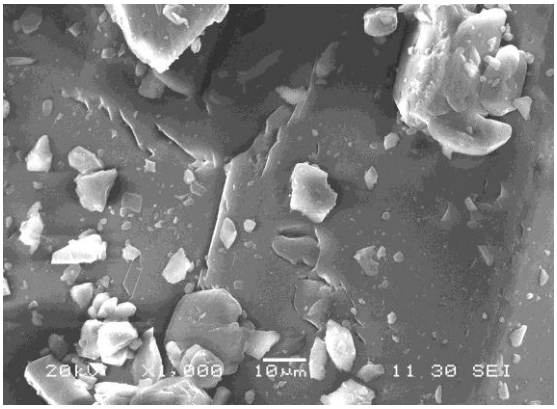

Fig. 14: SEM of Aceclofenac

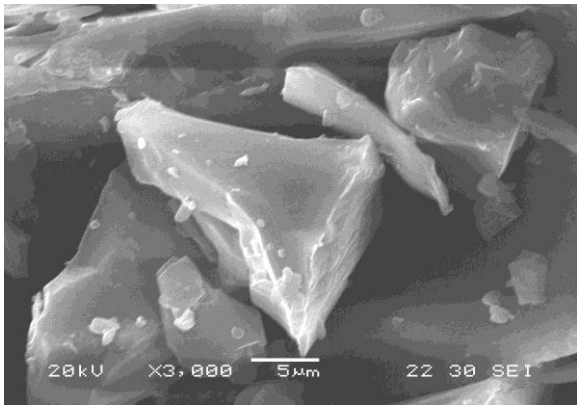

Fig.15: SEM of AE1

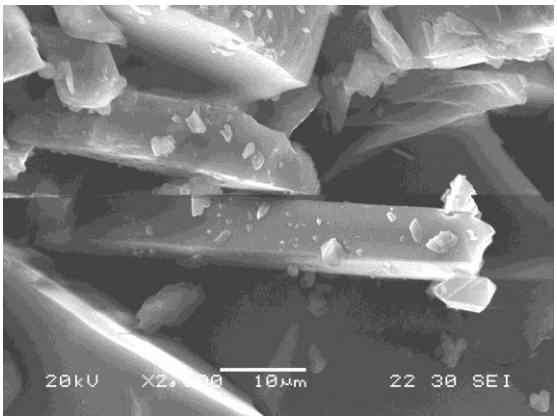

Fig. 16: SEM of AE4

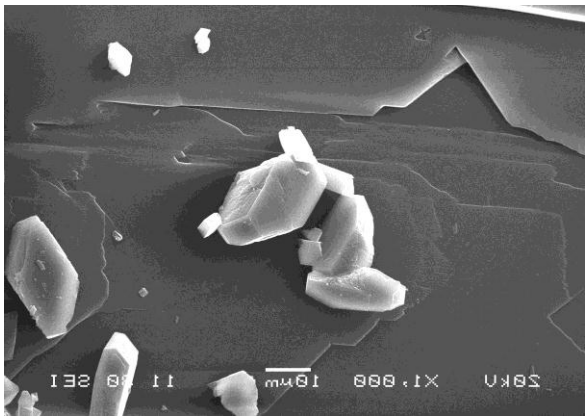

Fig. 17: SEM of AM3

Table 4: Crystallographic data for Pure Drug, AE2, AE4, AM3, & AM4

Crystallographic data	Pure Drug	AE2	AE4	AM3	AM4
Crystal system	Orthorhombic	Triclinic	Monoclinic	Hexagonal	Triclinic
Bravais type	P (Primitive)	P Primitive)	P Primitive)	P(Primitive)	P (Primitive)
Cell parameters	a=12.66 (2) Aº	a =10.699Aº	a = 20.30 Aº	a=22.802 Aº	a=10.517 Aº
	b = 8.87 (7) Aº	b =29.735Aº	b=17.936 Aº	b=22.802 Aº	b=10.958 Aº
	c = 8.46 (5) Aº	c=12.243 Aº	c = 13.39 Aº	c = 10.66 Aº	c = 9.909 Aº
	α = 90	α = 93.662	α = 90	α = 90	α = 103.166
	β = 90	β = 90.431	β = 103.687	β = 9	β = 99.496
	γ = 90	γ = 89.972	γ = 90	γ = 120	γ = 69.476

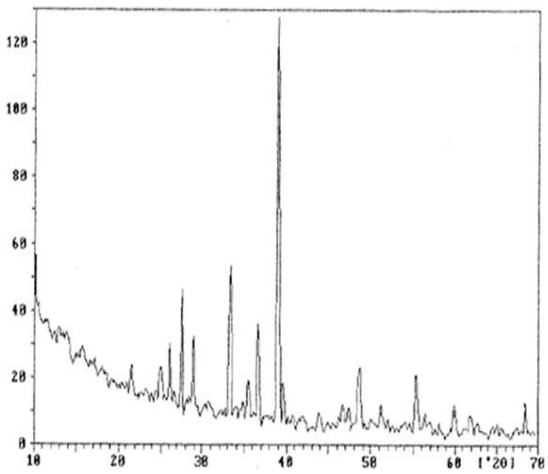

Fig. 18: X-ray diffraction of pure drug

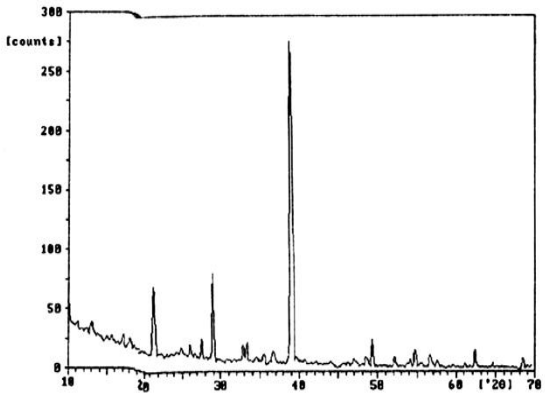

Fig.19: X-ray diffraction of AE2

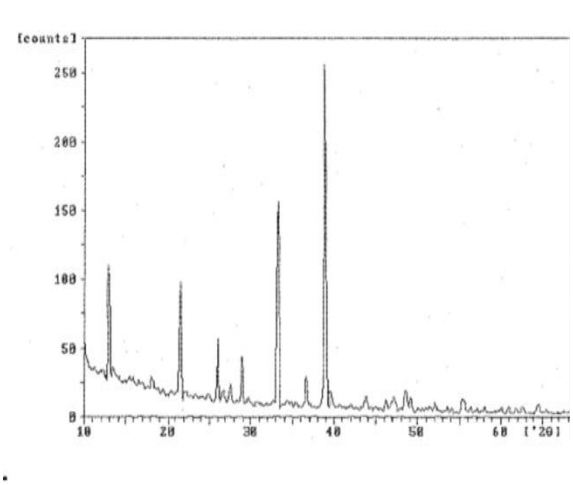

Fig. 20: X-ray diffraction of AE4

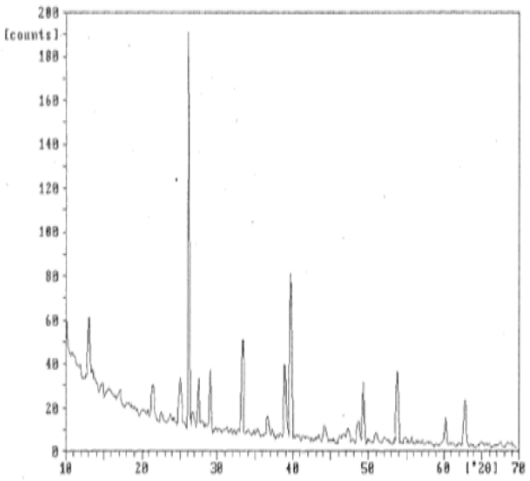

Fig. 21: X-ray diffraction of AM3

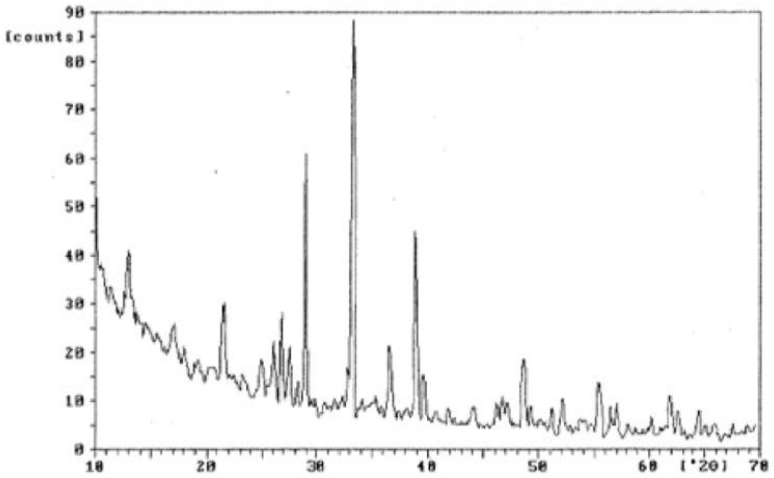

Fig. 22: X-ray diffraction pattern of AM4

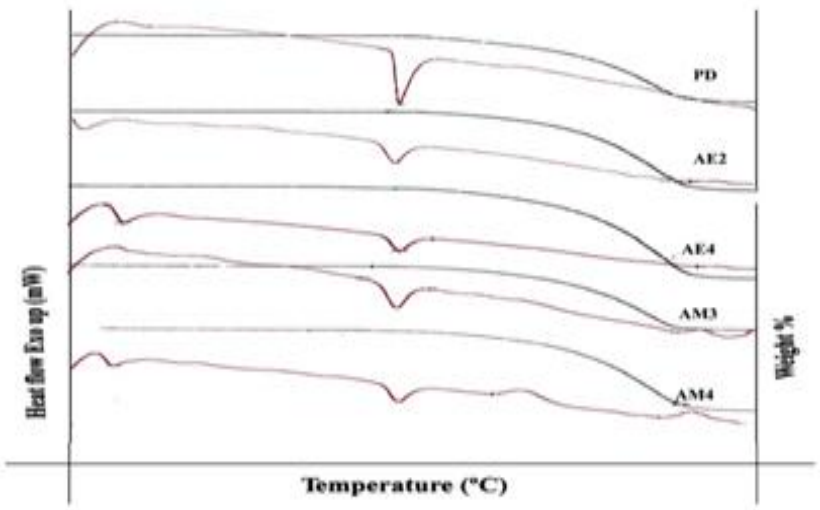

Fig. 23: DSC and TGA thermograms of pure drug (Aceclofenac) and prepared Aceclofenac crystals (AE2, AE4, AM3, AM4)

Table 5: Karl-Fischer Aquametry Data in terms of % Water Content

Sr No.	Formulation code	Crystal form	%water content
1.	Pure drug	Orthorhombic	2.162 ± 0.192
2.	AE2	Triclinic	0.656 ± 0.384
3.	AE4	Monoclinic	1.216 ± 0.333
4.	AM3	Hexagonal	1.081 ± 0.192
5.	AM4	Triclinic	0.811 ± 0.384

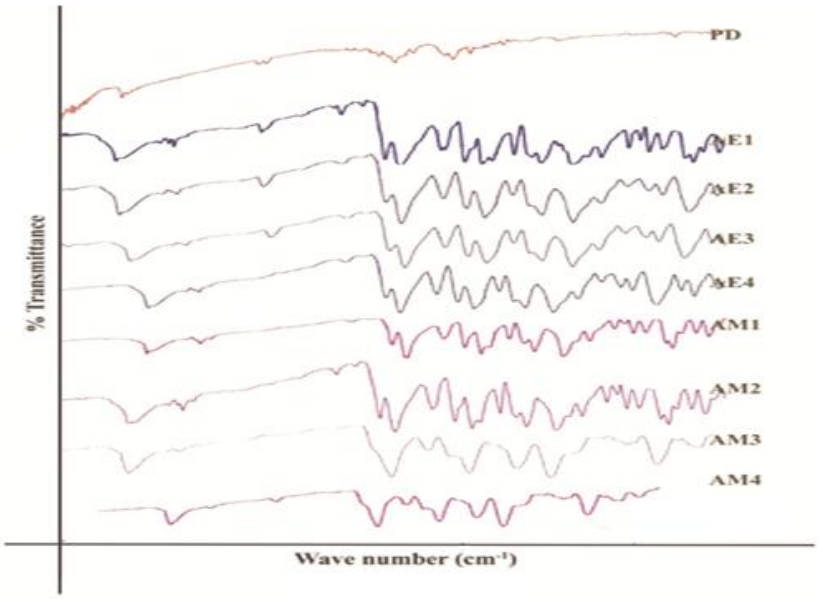

Fig. 24: FTIR spectra of pure drug (Aceclofenac) and prepared Aceclofenac crystals (AE1, AE2, AE3, AE4, AM1, AM2, AM3, AM4)

Table 6: Determination of melting point and loss on drying of prepared Aceclofenac crystals

Sr No.	Formulation code	Melting point (°C)		Loss on drying (%w/w)
		28.11.2009	13.12.2009	
1.	Pure drug	150	149	0.3
2.	AE1	148	152	0.36
3.	AE2	145	145	0.347
4.	AE3	148	151	0.361
5.	AE4	146	145	0.283
6.	AM1	147	144	0.279
7.	AM2	146	146	0.240
8.	AM3	148	149	0.28
9.	AM4	145	144	0.313

Table 7: Evaluation parameters of pure drug (Aceclofenac) and prepared Aceclofenac crystals

Formulation code	Appearance	Particle size (µm) (Mean±SD) (n=50)
Pure drug	Irregular shaped	30.48± 9.36
AE1	Spongy opaque	118.5± 31.08
AE2	Prismatic	121.03± 35.28
AE3	Spongy opaque	147.3± 39.62
AE4	Rod shaped	169.65± 36.70
AM1	Spongy	122.85± 33.26
AM2	Cone shaped	126.45± 30.64
AM3	Hexagonal	361.65± 116.18
AM4	Thin pole shaped	172.8± 31.99

Table 8: Solubility studies of prepared Aceclofenac crystals in distilled water

Sr. No.	Formulation code	Solubility (mg/ml) ±S.D	Fold increment
1.	Pure drug	0.085 ±0.02	--
2.	AE1	0.142 ± 0.04	1.66
3.	AE2	0.147 ± 0.06	1.72
4.	AE3	0.145 ± 0.01	1.70
5.	AE4	0.131 ± 0.03	1.54
6.	AM1	0.140 ± 0.03	1.64
7.	AM2	0.138 ± 0.04	1.61
8.	AM3	0.134 ± 0.04	1.57
9.	AM4	0.136 ± 0.03	1.49

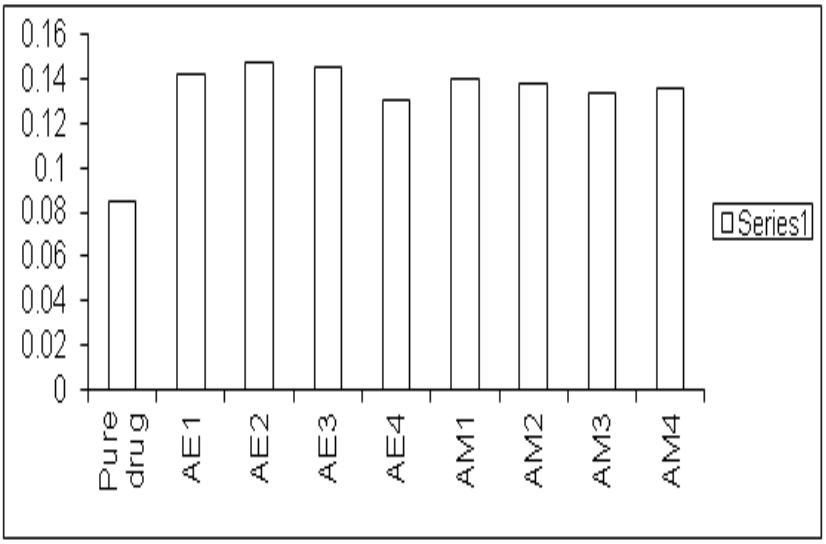

Fig. 25: Solubility studies of prepared Aceclofenac crystals in distilled water

Table 9: Dissolution profiles of pure drug (Aceclofenac) and prepared Aceclofenac crystals from ethanol and methanol

Time	Percentage drug release (mean±SD)								
	PD	AE1	AE2	AE3	AE4	AM1	AM2	AM3	AM4
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
15	11.34±0.17	21.46± 0.40	22.07± 0.29	21.80± 0.59	20.18± 0.24	19.91±0.18	20.31± 0.18	18.22± 0.19	19.64± 0.21
30	21.06±0.20	35.03± 0.11	35.84± 0.47	35.57± 0.40	31.79± 0.59	31.81±0.20	33.14± 0.24	30.57± 0.29	31.25± 0.24
45	29.56±0.24	45.96± 0.29	46.57± 0.24	46.30± 0.37	42.86± 0.35	42.39±0.42	43.26± 0.18	42.45± 0.36	42.39± 0.18
60	35.70±0.42	54.87± 0.52	55.62± 0.29	55.01± 0.24	52.31± 0.62	50.42±0.14	52.04± 0.27	52.58± 0.24	51.37± 0.23
75	40.43±0.24	63.11± 0.66	63.78± 0.15	63.45± 0.67	60.27± 0.18	57.57±1.00	59.94± 0.20	59.06± 0.91	59.47± 0.29
90	44.61±0.24	70.53± 0.89	71.21± 0.89	70.87± 0.89	67.50± 0.89	64.26±0.24	66.48± 1.47	65.81± 0.68	67.16± 1.17
105	48.06±0.44	76.95± 1.21	77.62± 1.16	76.61± 1.21	73.91± 1.47	70.76±0.70	71.88± 0.89	71.55± 0.58	73.24± 0.89
120	51.09±0.35	82.35± 1.47	83.02± 1.54	81.67± 1.47	78.63± 0.34	76.27±0.89	76.95± 1.17	76.61± 0.89	77.96± 1.22
135	53.79±0.30	85.72± 1.21	86.73± 0.58	85.38± 0.67	82.68± 1.34	81.67±0.34	81.67± 0.58	81.33± 0.68	81.79± 0.39
150	55.95±0.13	88.42± 1.35	89.43± 0.12	88.08± 0.58	86.06± 0.68	86.06±1.01	85.72± 0.89	85.05± 0.57	84.83± 0.70
165	57.57±0.29	90.78± 0.58	91.80± 0.58	90.11± 1.01	87.75± 0.59	89.43±0.68	89.1± 0.14	88.08± 0.89	86.52± 0.52
180	58.65±0.30	91.80± 0.33	92.47± 0.89	91.46± 0.67	88.42± 0.34	91.12±0.58	90.78± 1.47	89.43± 0.68	87.41± 0.69

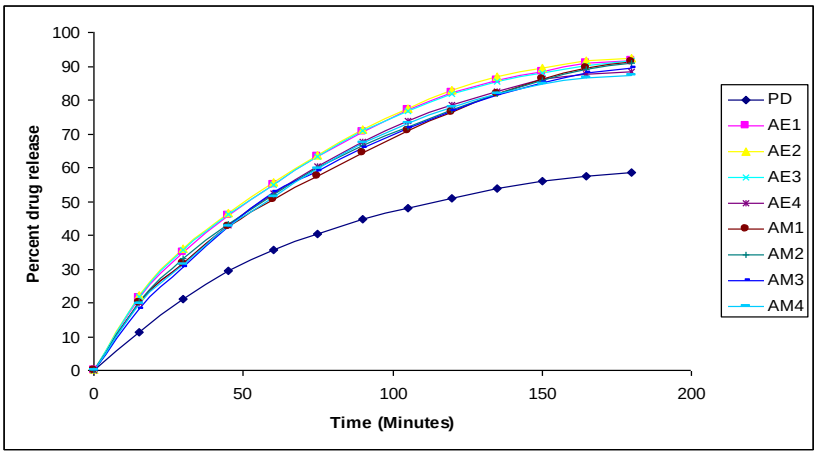

Fig. 26: Dissolution profiles of pure drug (Aceclofenac) and prepared Aceclofenac crystals from ethanol and methanol

Table 10: Evaluation of flow properties of obtained Aceclofenac crystals:

Sr. No.	Formulation code	Angle of Repose (θ)	Bulk Volume	Tapped Volume	Bulk Density (g/cm³)	Tapped density (g/cm³)	Hausner's Ratio	Compressibility index (%)
1.	DAC	23.74	7.02	6.00	0.41	0.48	1.170	14.58
2.	DAE1	22.78	7.16	5.8	0.4022	0.4965	1.234	18.99
3.	DAE2	24.22	6.8	6.00	0.4235	0.4813	1.136	11.96
4.	DAE3	21.80	7	6.2	0.4114	0.4645	1.1290	11.43
5.	DAE4	25.17	7.3	6.2	0.3945	0.4645	1.1774	15.06
6.	DAM1	23.74	8.8	6.4	0.4235	0.45	1.0625	16.06
7.	DAM2	26.56	7.1	5.8	0.4056	0.4965	1.2241	18.30
8.	DAM3	21.80	6.9	6.2	0.4173	0.4645	1.113	10.16
9.	DAM4	25.69	7.1	6.2	0.4056	0.4645	1.145	12.68

DISCUSSION

In the present investigation, the solubility was determined in different organic solvents for selection of solvents. So the calibration curves were taken in ethanol and methanol as reported in the literature. Because of dissolution study was performed in the pH 7.4 phosphate buffer, the calibration curve in the pH 7.4 phosphate buffer was taken. The results of DSC studies are given in Fig.23. Pure Aceclofenac showed a sharp endotherm at 151.22^{0}C corresponding to its melting point. There was no appreciable change in the melting endotherms of the prepared crystals (AE2 = 151.22^{o}C, AE4 = 149.76^{o}C, AM3 = 149.76^{o}C, AM4 = 149.76^{o}C,) as compared to pure drug. However, there was slight decrease in the melting point of drug when prepared in the form of crystals. TGA studies indicated that the water content of the pure drug (Aceclofenac) was around 2% while other prepared crystals showed water contents varied from 0.5 to 1%. TGA analysis indicated less than 5.12% water content. Hence pure drug and prepared crystals ruled out hydrate formation. Water contents for these crystal forms were determined by Karl Fischer aquametry the pure drug showed maximum water content of 2.162%±0.192 while prepared crystals showed approximately water content in the range of 0.5 to 1.21%.

The melting point of pure drug and all prepared crystals were within the range of 144-152^{0}C. The LOD values of crystals prepared with addition of additives ranged between 0.1-0.173 %.The prepared crystals showed increased solubility as compared to commercial pure drug (0.0855 ± 0.002mg/ml). The maximum solubility was observed in AE2 (Aceclofenac + ethanol i.e. 0.147 ± 0.06mg/ml.

The Recrystallization of pure drug from various solvents, showed increase in the dissolution rate of different modified crystals (AE1= 91.8± 0.338%, AE2= 92.475± 0.892%, AE3=91.463± 0.675%, AE4= 88.425± 0.338%, AM1= 91.125± 0.584%, AM2= 90.787± 1.47%, AM3= 89.437± 0.675%, AM4= 87.413± 0.675%) than pure drug (58.657± 0.309%). The angle of repose of pure drug and recrystallize Aceclofenac was within the range of 21.80 to 26.56 which is less $\leq 30^0$ indicating a free flowing material. The Carr's Index was in the range of 11 to 15% and Hausner's Ratio is between 1.12 to 1.18.

CONCLUSION

The study conducted so far showed encouraging results of improved solubility because of effects of change in solid-state properties by Recrystallization process on properties of Aceclofenac Pure drug. Recrystallization of aceclofenac resulted in the increase of

dissolution rate of different modified crystals than pure drug due to better crystallinity of modified crystals with the addition of polymer, the dissolution rate was further increased due to adsorption of polymers on the crystal surface and which in terms may improves bioavailability.

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