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DESIGN DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLETS CONTAINING SOLID DISPERSION OF ACOTIAMIDE

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Abstract:
In the present study, an attempt was made to develop fast-dissolving tablets containing solid dispersion of NSAID by using PVP K30 as a carrier and crospovidone and croscarmellose sodium as a super disintegrant. From data obtained from the formulation and evaluation of the dissolving tablet, the following conclusions were made:
The solid dispersions of Acotiamide were prepared by physical mixture and solvent evaporation method using PVP K 30 as a carrier in the ratio of 1:3, 1:5, and 1:7 weights respectively. The solubility and dissolution rate of Acotiamide from solid dispersion (SE3) was increased in the presence of PVP K 30 as that of pure Acotiamide drug. Among the two methods, the solvent evaporation method is better efficient than the physical mixture method. PVP K 30 proved to be a good carrier for the preparation of solid dispersion of poor water soluble drug.US Food and Drug Administration (USFDA) defined fast dissolving tablet as "A solid dosage form encompassing active ingredient or medical ingredients which disintegrates fast within a substance of seconds when placed upon the tongue." The disintegration time for fast-dissolving tablets ranges from a few seconds to a few minutes. Also, United state Pharmacopoeia approved this dosage form as an orally disintegrating tablet. European pharmacopeia defines identical terms, or dispersible tablets, that disperse rapidly within 3 minutes in the mouth before swallowing. Over a decade, the demand for the development of fast-dissolving tablets has tremendously increased because it has an impact on the patient's compliance.

Keywords: *Acotiamide, Solid Dispersion, Fast Dissolving,*

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INTRODUCTION:

The effectiveness of the drug is depending upon the ability of the dosage form to deliver the medicament to its site of action at a rate and amount sufficient to elicit the desired pharmacological response. This property of dosage form is referred to as physiologic availability, biologic availability, or simply bioavailability. Thus the term bioavailability is defined as the rate and extent of unchanged drug from its dosage forms.[1] The In-vivo performance of orally administered drugs depends upon their solubility and tissue permeability characteristics. BCS is a scientific framework for classifying drug substances according to their aqueous solubility and permeability. BCS guidelines are provided by U.S. Food and Drug Administration (USFDA), the World Health Organization(WHO), and European Medicines Agencies (EMEA). According to BCS classification, drug substances are grouped into four major classes

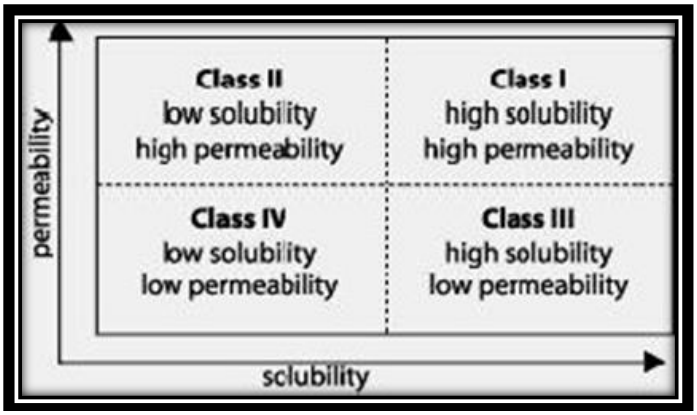

Fig. No. 1: The Biopharmaceutics Classification System

Class I: (High Solubility, High Permeability)

Drugs under this class are well absorbed and their absorption rate is higher than excretion. The rate-limiting step is dissolution and if drug dissolution is very rap id then gastric emptying time is rate limiting
Examples: verapamil, Metaprolol, Diltiazem

Class II: (Low solubility, High Permeability)

The bioavailabilities of these drugs are depending upon the solvation rate. The absorption rate of class II drugs is slower than class I drugs.
Example: Ketocanazole, Mefenamic acid, Itraconazole

Class III: (High solubility, low permeability)

The absorption is limited by the permeation rate but the drug is solvated very fast. The drug is exhibit high variation in the rate and extent of drug absorption.
Example: Cimetidine, Captopril

Class IV: (Low solubility, low permeability)

These compounds have poor bioavailability and are not good to absorbed to entire gastrointestinal tract
Example: Hydrochlorothiazide, taxol[2]
The rate-limiting step for the bioavailability and absorption of active pharmaceutical ingredients is the release of medicament from its dosage forms or drug permeation through the biological membrane. Drugs having high solubility and high permeability (class I), release from dosage forms occur very rapidly then gastric emptying time will be a rate-limiting step for drug absorption. Whereas drugs have low solubility and high permeability (class II), release from dosage forms occurs slowly. In-vivo drug dissolution is a rate-limiting step for the absorption of class II drugs. Class II drugs exhibited variable bioavailability and need enhancement of dissolution to increase drug bioavailability. There are various methods of enhancement of bioavailability.

NEED:

In the present research work, fast-dissolving tablets of Acotiamide are prepared by using the solid dispersion technique, and various super disintegrants like crospovidone, croscarmellose sodium are used with the direct compression method.

- To prepare solid dispersion of Acotiamide using PVP –K 30 as a carrier
- To evaluate prepared solid dispersion by drug content uniformity, % practical yield, Solubility study, in vitro dissolution study, FT-IR studies, etc.
- To study the pre-formulation parameters like bulk density, tapped density, Carr's index, Hausner's ratio, angle of repose, etc.
- To formulate fast-dissolving tablets containing solid dispersion of Acotiamide

using super disintegrants in different proportions by direct compression method.

Drug profile:
Acotiamide

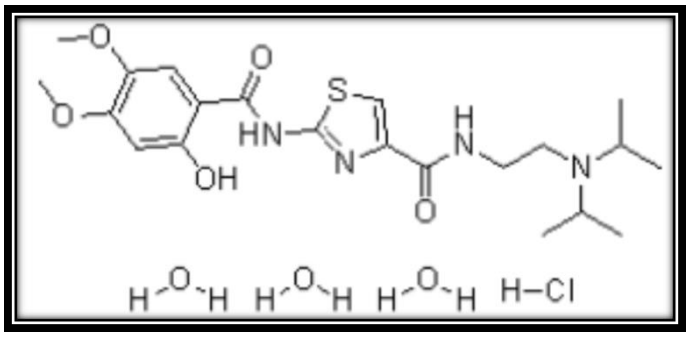

Fig No.2:Chemical Structure of Acotiamide.

MATERIALS:

Table. No.1: List of ingredient

Sr. No.	Name of the ingredient
1	Acotiamide
2	PVP K-30
3	Crospovidone
4	Croscarmellose
5	Microcrystelline
6	Lactose
7	Magnesium stearate
8	Sodium saccharine
9	Talc

EXPERIMENTAL WORK:

Selection of Drug and Excipients:
In the present work, poorly water-soluble non-steroidal anti-inflammatory drugs viz Acotiamide are selected. Acotiamide is used in the treatment of rheumatoid arthritis, acute gouty arthritis, spondylitis, and osteoarthritis. The drug is practically insoluble and highly permeable.

Preformulation Study of Drug:
Melting point determination:
The melting point of pure Acotiamide was determined by the open capillary method. The capillary tube was closed at one end by fusion and was filled with Acotiamide and placed in Thiele's melting point apparatus and the temperature at which the drug melted was noted. The average of triplicate readings was noted and compared with the literature value.

Determination of max of Acotiamide in phosphate buffer 6.8:
100 mg of pure drug was transferred into 100 ml of phosphate buffer 6.8 in a volumetric flask. Withdrawn 10 ml sample from this solution and diluted to 100 ml it makes 100mcg/ml(stock solution) then concentration make by withdrawing 1 ml from the stock solution and diluting to 100 ml makes the solution of concentration 10 g/ml. Finally, the standard solution (10µg/ml) of Acotiamide in phosphate buffer pH 6.8 was scanned between 200-400 nm on a UV- visible spectrophotometer to record the wavelength of maximum absorption (λ max).

Determination of calibration curve of Acotiamide in phosphate buffer 6.8:
100 mg of pure drug was transferred into 100 ml of phosphate buffer 6.8 in a volumetric flask. Withdrawn 10 ml sample from this solution and diluted to 100ml it makes 100 mcg/ml(stock solution) then concentration make by withdrawing 0.5,1,1.5,

2, 2.5, 3,3.5,4,4.5,5ml from the stock solution and diluted to 100 ml it makes the solution of concentration 5 g/ml,10 g/ml,15 g/ml,

Differential scanning calorimetry (DSC)
DSC was performed to assess the thermotropic properties and thermal behavior of the drug (Acotiamide). A differential scanning calorimetry thermogram of the pure drug was recorded on a thermal analyzer. The samples were heated from 25 to 500 °C at a heating rate of 10 °C/min in an inert nitrogen atmosphere.

Fourier Transform Infra-Red (FTIR) Spectroscopy:
The infrared spectrum of Acotiamide was determined on a Fourier Transform Infrared spectrophotometer Small quantity of sample was taken and directly put on the IR platform. Then the spectra were scanned over a wavelength region of 4000 to 400 cm-1 at a resolution of 4 cm1.

Method of Preparation of Solid Dispersion Systems:
a. Solvent Evaporation Method:
An accurate amount of Acotiamide and carrier was dissolved in a minimum quantity of ethanol with continuous stirring. The solvent was removed at 45oc -400c until the solid dispersion was dry. The dried mass was pulverized, passes through a 100 mesh sieve, and was stored in desiccators until used for further studies.

b. Physical mixture:
Physical mixtures were prepared by mixing Acotiamide with PVP K -30 for three minutes in a mortar until a homogeneous mixture was obtained. The resulting mixture was sieved through sieve no. 100 and then stored in desiccators at room temperature until use.

Method of Preparation of Fast-Dissolving Tablets:
In this work, a direct compression method with the aid of super disintegrants was attempted for the formulation development of fast-dissolving tablets containing solid dispersion of Acotiamide. The promising solid dispersion formulations were further formulated as fast-dissolving tablets using suitable super disintegrants. A dose of 25 mg is selected for the present study.

The development of fast dissolving tablets formulation in the present study was based on the type and concentration of super disintegrants. Two different super disintegrants were used in different concentrations to get a tablet with good physical properties. The formulation design of fast-dissolving tablets of Acotiamide

Table No.2: Formulation of fast-dissolving tablets containing Acotiamide solid dispersion formulation (PM3

Ingredients (mg)	TP1	TP2	TP3	TP4	TP5
Amount of solid dispersion equivalent to 25 mg	200	200	200	200	200
Microcrystalline cellulose	80	80	80	80	80
Crospovidone			16	20	10
Croscarmellose sodium	16	20			10
Sodium saccharine	3	3	3	3	3
Magnesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Lactose	95	91	95	91	91
Total	400	400	400	400	400

Table No.3: Formulation of conventional tablets of Acotiamide by direct compression method

Ingredients (mg)	Qty
Acotiamide	25
Microcrystalline cellulose	80
Sodium saccharine	3
Magnesium stearate	3
Talc	3
Lactose	q.s.

Preparation of fast-dissolving tablets of Acotiamide by direct compression method:

Fast-dissolving tablets of Acotiamide were prepared by direct compression method according to the

formula given in tables no.8 and 9. All the ingredients were passed through a 40-mesh sieve separately. The solid dispersion containing 25 mg Acotiamide and diluents was mixed by a small portion of both each time and blending I to get a uniform mixture then other ingredients were mixed in geometrical order. The prepared blend was compressed (10mm Punch) using a multi-station tablet press machine (Shakti, Ahmadabad, India).

Evaluation of Fast Dissolving Tablets:

I. Pre-compression parameters:

Determination of the angle of repose, Carr‟s index, and Hausner‟s ratio were used to characterize flow properties of the solid dispersion systems. The flow ability of a powder is of critical importance in the production of pharmaceutical dosage forms to get a uniform feed as well as reproducible filling of tablet dies, otherwise, high dose variation will occur.

1) Angle of repose:

The angle of repose has been used as indirect methods of quantifying powder flow ability. Angle of repose is defined as the maximum angle possible between the surface of pile of the powder and horizontal surface the frictional force in a loose powder or granules can be determined by angle of repose. Angle of repose for blend of each formulation was determined by fixed funnel method. The funnel is secured with its tip with height h, above a plane of paper kept on a flat horizontal plane .The powders were poured through the funnel until the apex of the conical pile so formed just reaches the tip of funnel. The angle of repose was determined by substituting the values of the base radius „r ‟and height of the pile „h‟ in the formula given below,

Table No.4: Relation between angle of repose ( ) and flow properties

Angle of repose (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

2) Bulk density:

Bulk density was determined by pouring pre-sieved drug and excipients blend into a graduated cylinder and measuring the volume and weight “as it is”. It is expressed in g/ml and is given by

3) Tapped density:

It was determined by placing a graduated cylinder, containing a known mass of drug-excipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml and is given by

4) Carr’s Index (%Compressibility):

The compressibility index and Hausner ratio are measures of the property of powder to be compressed. The packing ability of drug was evaluated from volume change, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr‟s compressibility index was calculated as follows.

5) Hausner Ratio:

It is measurement of frictional resistance of the drug. He showed that the powder with low inter particle friction had ratio of approximately 1.2,whereas more cohesive less free flowing powder has Hausner‟s ratio greater than 1.6 . Hausner‟s ratio less than 1.25 indicate good flow properties. It was determined by the ratio of tapped density and bulk density

II. Post-compression Parameters:

Prepared tablets were subjected to evaluation of different properties including tablet hardness, friability, uniformity of thickness, In vitro disintegration time, In vitro dissolution test, etc.

1) Hardness:

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using a Monsanto hardness tester. It is expressed in Kg/cm2. Three tablets were randomly picked and mean hardness of the tablets formulation was determined.

2) Friability:

Tablet hardness is not an absolute indicator of strength, since some formulations compressed into very hard tablet tend to cap on attrition losing their crown potions. Therefore another measure of tablet strengths, its friability is often measured. The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again.

3) Weight Variation Test:

The weight of tablets is measured to ensure that a tablet contain the proper amount of drug. Twenty tablets were selected at random and the average weight was determined.

USP official limits of percentage deviation of tablet are presented in the table no. 13

Average weight of tablet Percent deviation

4) Uniformity of Thickness:

The thickness of the tablets was determined using a vernier caliper. Three tablets from each type of formulation were used and average values were calculated. It is expressed in mm.

5) Uniformity of Drug Content:-

Five tablets of each type of formulation were weighed and crushed in mortar and powder equivalent to 25 mg of drug transferred in conical flask containing 25 ml phosphate buffer 6.8. Its concentration 1000mcg/ml.10 ml from this stock solution was taken and diluted to 100 ml phosphate buffer 6.8.; it makes 100 g/ml. Then 25 g/ml solution prepared by taking 2.5 ml from this stock solution and diluted up to 10 ml. Absorbance measured at 319 nm.

6) Wetting Time:

A piece of tissue paper folded twice containing was placed in a small Petri dish (ID =6.5 cm) containing 10 ml of phosphate buffer 6.8, a tablet was put on the paper and the time required for complete wetting was measured as wetting time. The study was performed in triplicate.

7) In -vitro disintegration time:

Generally accepted maxima is that for a drug to be readily available to the body, it must be in solution form. For most of the tablets the first important step toward solution is breakdown of the tablet into smaller particles, a process known as disintegration. In vitro disintegration time is measure using is integration test apparatus as per I.P. specifications. I.P. specifications: Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using phosphate buffer 6.8 maintained at 370±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 370±2°C. The time in seconds taken for complete disintegration of tablet with no palpable mass remaining in the apparatus was measured and recorded. The assembly was removed from liquid.

8) In-vitro dissolution study

The release rate of Acotiamide from fast dissolving tablets was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer 6.8 dissolution medium, at 37±0.5°C and 50 rpm. Sample volume of 5 ml was withdrawn at every 1 minute time interval and filtered. The volume withdrawn was replaced by fresh volume of dissolution medium to maintain constant volume of medium. The filtered samples were analyzed spectrophotometrically at 319 nm using phosphate buffer 6.8 as a blank.

9) Differential scanning calorimetry (DSC) of fast dissolving tablets:

DSC was performed in order to assess the thermotropic properties and thermal behavior of oral fast dissolving tablets prepared. Differential scanning calorimetry thermograms of optimized tablet formulation were recorded on a thermal analyzer. The samples were heated from 25 to 500 °C at a heating rate of 10 °C/min in an inert nitrogen atmosphere.

10) Fourier Transform Infra-Red (FTIR) Spectroscopy of fast dissolving tablets:

IR spectroscopy is one of the qualitative analytical techniques, which offers the possibility of detecting chemical interaction. Infrared spectra of optimized formulations were determined on Fourier Transform Infrared Spectrophotometer using KBr dispersion method. The base line correction was done using dried potassium bromide. Then the spectrum of physical mixture of drug and potassium bromide was recorded.

RESULTS AND DISCUSSION:

Preformulation Study of Drug:

Melting Point-

The melting point of Acotiamide was found to be 1610c which complies with range that given in the literature i.e. 158-1620c.

Determination of λ max of the Acotiamide-

The standard solution of Acotiamide shows maximum absorbance at 319 nm wavelength in spectroscopy.

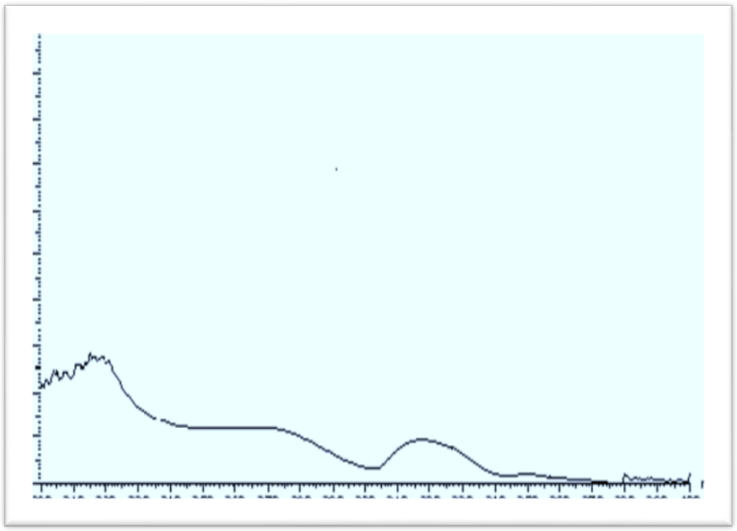

Fig. No.3: UV spectrum of Acotiamide

Preparation of standard calibration curve of Acotiamide

The standard calibration curve of Acotiamide in phosphate buffer pH 6.8 at 319 nm was plotted using various concentrations ranging from 2-50 g/ml,

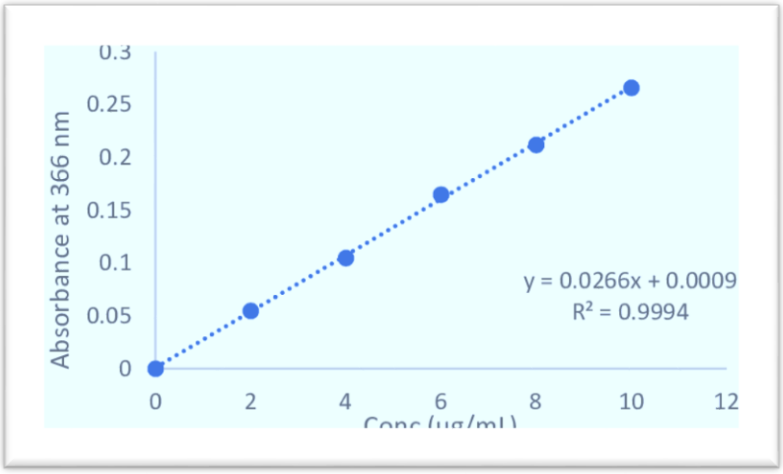

Fig. No.4: Standard calibration curve of Acotiamide in pH 6.8 phosphate Buffer at 319nm

Table. No.5: Observations for standard calibration curve of Acotiamide in pH 6.8 phosphate buffer at 319 nm66

Sr. no	Concentration	Absorbance
1	0	0
2	5	0.0084
3	10	0.1859
4	15	0.2637
5	20	0.3545

6	25	0.4573
7	30	0.5574
8	35	0.6325
9	40	0.7184
10	45	0.8147
11	50	0.9158

Table. No.6: Standard curve statistics

Sr. No	Parameters	Observations
1	Absorbance maximum	319
2	Slope	0.0018
3	Intercept	-0.023
4	Coefficient of correlation	0.994

Differential scanning calorimetry (DSC):

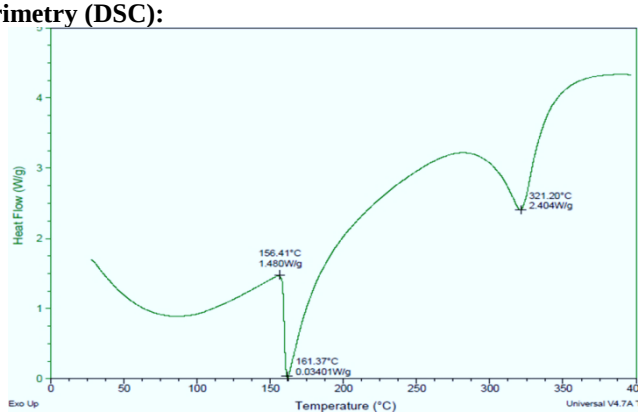

Fig. No 5: DSC of Pure Acotiamide

The DSC thermogram of Acotiamide has presented in Fig. no.5 The DSC thermograms of Acotiamide depict a sharp endothermic peak at 161.370c. Such a sharp endothermic peak signifies that Acotiamide used was in a pure state.

Fourier Transform Infra-Red (FTIR) Spectroscopy:

An IR spectrum of Acotiamide is presented in Figure no 18. Observed peaks are shown in table no.7 these peaks are similar to the reported peaks of Acotiamide.

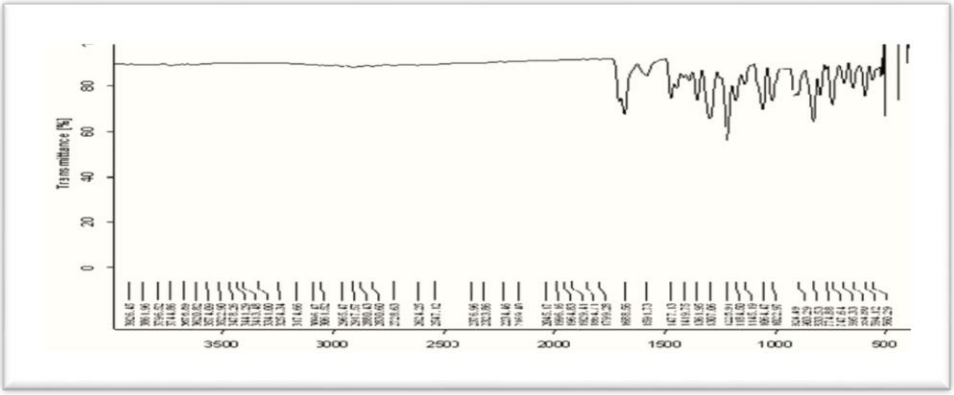

Fig. No.6: FTIR Spectrum of Pure Acotiamide

From the data obtained it was observed that characteristic peaks appear with identical or with minor differences, at frequencies 1688.56cm-1 (C=O in ketone), 1477.13cm-1 (OH in –COOH group), 1307.06cm-1(C=O in COOH group), 1145.11 (C=C in aromatic alkenes

Table No.7: Physical parameters of Acotiamide solid dispersion

Formulation Code	Physical Appearance	
	Color	Appearance
PM1	White	Fine powder
PM2	White	Fine powder
PM3	White	Fine powder
SE1	Light yellow	Fine powder
SE2	Light yellow	Fine powder
SE3	Light yellow	Fine powder

A) Drug content uniformity of Acotiamide solid dispersion:

Table No.8: Drug content, Percent practical yield, solubility study of Acotiamide solid dispersion:

Formulations	Drug content Uniformity (%) SD	% Practical Yield	Solubility in PBS 6.8 (g/ml) SD
ID	-	-	0.5203 ± 0.008
PM1	79.56 ± 0.13	90	1.081 ± 0.08
PM2	88.39 ± 0.13	100	1.059 ± 0.07
PM3	98.65 ± 0.17	100	1.464 ± 0.01
SE1	97.43 ± 0.17	54	1.602 ± 0.002
SE2	98.86 ± 0.47	68	1.860 ± 3.02
SE3	99.59 ± 0.13	92	3.339 ± 0.05

The drug content of all six formulations is shown in table no.8 The Drug content of all six formulations was found to be in the range of 79.56-99.59%. The maximum % drug content was found in formulation SE3.

B) % practical yield of Acotiamide solid dispersion :

The % practical yield of all six formulations are shown in table no.18 .The % practical yield of all six formulations was found to be in the range of 54% to 92%. The maximum % practical yield was found to be 92 % in SE3.

C) Solubility study of Acotiamide solid dispersion:

Proportions of PVP K- 30 increased, and the solubility of Acotiamide also increases. All the solid dispersions show higher solubility as compared to pure Acotiamide.

D) Differential scanning calorimetry (DSC) studies of Acotiamide solid dispersion:

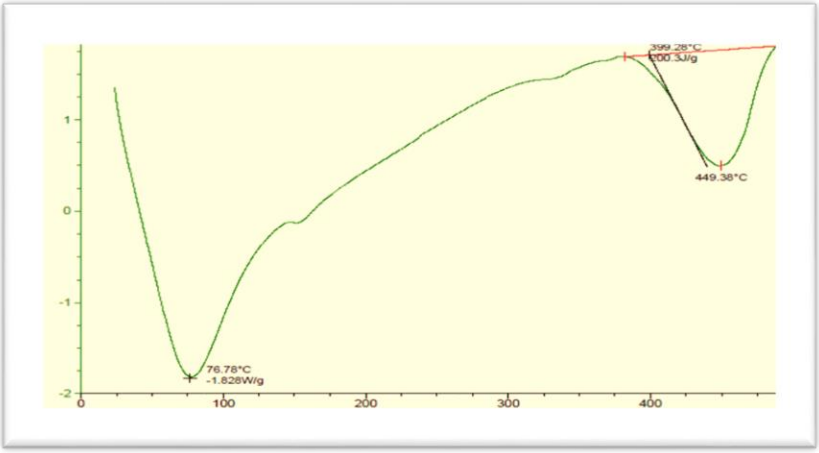

Fig. No.7: DSC of Acotiamide solid dispersion formulation (PM3)

E) Fourier Transform Infrared spectroscopy studies of Acotiamide solid dispersion:

Table No.9: Observed peaks of FTIR spectra of Acotiamide solid dispersion

Functional group	Observed wave number (cm^{-1})
C=O in ketone	1684.02
OH in –COOH group	1449.40
C=O in COOH group	1362.36
C=C in aromatic alkene	1145.77

Evaluation of Solid Dispersion Incorporated Acotiamide Fast Dissolving Tablet and Conventional Tablet:

I. Results of Pre-compression Parameters:

Pre-compression parameters play an important role in improving the flow properties of pharmaceuticals, especially in tablet formulations. These include angle of repose, bulk density tapped density, Hausner's ratio, and Carr's index. Acotiamide fast-dissolving tablets i.e. TP1 to TP5 tablets formulations prepared by using PM3 solid dispersion whereas TS1 to TS5 tablet formulations are prepared by SE3.

Table No.10: Results of Pre-Compression Parameters:

Formulation code	The angle of repose (degrees)	Bulk Density g/cc	Tapped Density g/cc	Hausner's Ratio	Carr's Index %
CT	22.45 ± 0.11	0.421±0.15	0.478 ± 0.23	1.09 ± 0.01	12.35 ± 1.35
TP1	16.18 ± 0.66	0.450±0.13	0.492 ± 0.15	1.09 ± 0.02	8.36 ± 2.13
TP2	20.00 ± 0.90	0.418±0.19	0.502 ± 0.15	1.10 ± 0.05	9.53 ± 0.45
TP3	22.90 ± 0.24	0.466±0.10	0.455 ± 0.08	1.15 ± 0.08	9.68 ± 1.99
TP4	20.47 ± 0.90	0.547±0.14	0.503 ± 0.05	1.14 ± 0.02	12.99 ± 2.17
TP5	21.56 ± 0.91	0.739±0.29	0.665 ± 0.14	1.09 ± 0.02	8.48 ± 2.32
TS1	17.98 ± 0.69	0.466±0.24	0.444 ± 0.11	1.19 ± 0.02	9.73 ± 2.38
TS2	19.02 ± 0.30	0.478±0.34	0.545 ± 0.12	1.09 ± 0.02	8.91 ± 1.69
TS3	21.29 ± 0.57	0.581±0.21	0.637 ± 0.13	1.12 ± 0.01	10.83 ± 1.4
TS4	20.67 ± 0.35	0.814±0.49	0.532 ± 0.11	1.12 ± 0.03	11.33 ± 2.5
TS5	21.80 ± 0.39	0.525±0.30	0.502 ± 0.13	1.08 ± 0.03	8.18 ± 2.61

II. Result of Post-Compression Parameters:

Table No.11: Results of post-compression parameters for the tablets like hardness, friability, weight variation, and uniformity of thickness:

Formulation code	Hardness Kg/cm_2 *(N)*	Friability %	Weight Variation mg	Uniformity of thickness (mm)
CT	3.2 ± 0.2	0.51	396 ± 0.62	3.2 ± 0.15
TP1	3.2 ± 0.2	0.64	397 ± 0.48	3.3 ± 0.20
TP2	3.2 ± 0.2	0.47	397 ± 0.90	3.2 ± 0.11
TP3	3.2 ± 0.31	0.66	396 ± 0.90	3.1 ± 0.17
TP4	3.1 ± 0.11	0.40	395 ± 0.55	3.2 ± 0.1
TP5	2.9 ± 0.23	0.52	396 ± 0.70	3.2 ± 0.15
TS1	3.1 ± 0.05	0.68	397 ±.1.06	3.2 ± 0.11
TS2	3.1 ± 0.11	0.54	397 ± 1.22	3.4 ± 0.41
TS3	3.0 ± 0.2	0.32	396 ± 0.85	3.1 ± 0.15
TS4	3.0 ± 0.23	0.41	396 ± 0.80	3.2 ± 0.11
TS5	3.0 ± 0.30	0.32	395 ± 0.99	3.2 ± 0.15

All values are expressed as mean ± SD, n=3

2) In- Vitro dissolution studies:

Table No.12: Cumulative % drug release profile of TP1, TP2, TP3, TP4, TP5

Time (min)	Cumulative % drug release				
	TP1	**TP2**	**TP3**	**TP4**	**TP5**
0	**0**	**0**	**0**	**0**	**0**
1	43.99 ± 1.05	62.98 ± 0.16	59.77 ± 0.6	64.95 ± 0.14	64.74 ± 0.38
2	46.93 ± 0.61	68.27 ± 0.18	68.85 ± 0.9	67.79 ± 0.16	70.94 ± 0.33
3	70.94 ± 0.33	59.37 ± 0.83	70.12 ± 0.14	73.98 ± 0.12	74.85 ± 0.32
4	49.53 ± 0.10	71.09 ± 0.18	72.86 ± 0.37	78.97 ± 0.14	84.75 ± 0.28
5	59.11± 0.17	83.78 ± 0.15	74.22 ± 0.12	86.50 ± 0.14	87.67 ± 0.26
6	62.19 ± 0.11	85.03 ± 0.17	79.02 ± 0.19	95.03 ± 0.15	89.79 ± 0.17
7	72.42 ± 0.25	87.38 ± 0.14	84.14 ± 0.14	97.76 ± 0.18	92.77 ± 0.26
8	83.63 ± 0.25	92.78 ± 0.18	90.95 ± 0.19	99.41 ± 0.18	95.43 ± 0.21
9	84.74 ± 0.36	96.77 ± 2.79	98.70 ± 0.34	-	99.63 ± 0.14
10	89.74 ± 0.10	98.52 ± 0.17	99.37 ± 0.14	-	-
11	96.99 ± 0.13	-	-	-	-

All values are expressed as mean ± SD, n=3

3) Differential scanning calorimetry (DSC):

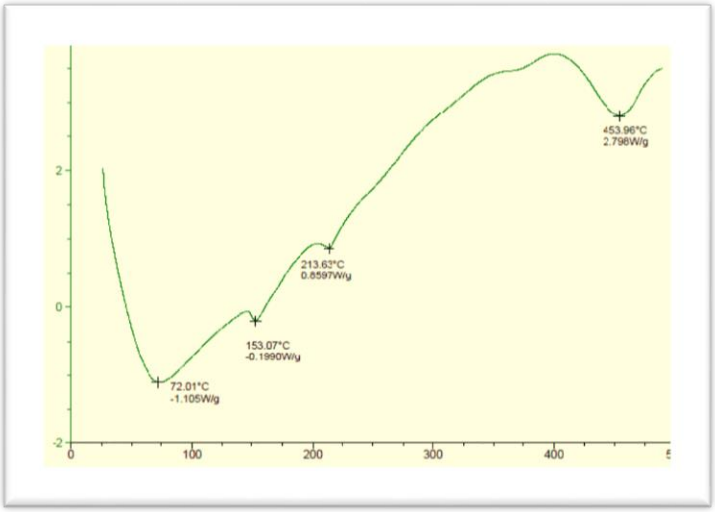

Fig. No.8: DSC of Optimized formulations of fast-dissolving tablets

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4) Fourier Transform Infra-Red (FTIR) Spectroscopy

Table No.13: Observed peaks of FTIR spectra of optimized formulation of fast-dissolving tablets containing solid dispersions of Acotiamide

Functional group	wave number (cm^{-1})
C=O in ketone	1684.02
OH in –COOH group	1449.40
C=O in COOH group	1364.36
C=C in aromatic alkene	145.77

The FTIR spectra of optimized formulations of fast-dissolving tablets (TS4) containing solid dispersions of Acotiamide showed characteristic distinct peaks with approximately the same intensity. Thus, there is no interaction between the drug and polymers as shown in fig. no.8. FTIR spectra of optimized formulations of fast-dissolving tablets containing solid dispersions of Acotiamide indicated that the drug is compatible with all the excipients.

Table No.14: Observed peaks of FTIR spectra of optimized formulation of fast dissolving

Functional group Observed	wave number (cm^{-1})
C=O in ketone	1645.29
OH in –COOH group	1461.06
C=O in COOH group	1338.15
C=C in aromatic alkene	1162.89

SUMMARY AND CONCLUSION:

The solid dispersions of Acotiamide were prepared by physical mixture and solvent evaporation method using PVP K 30 as a carrier in the ratio of 1:3, 1:5, and 1:7 weights respectively. The solubility and dissolution rate of Acotiamide from solid dispersion (SE3) were increased in the presence of PVP K 30 as that of pure Acotiamide drug. Among the two methods, the solvent evaporation method is better efficient than the physical mixture method. Pvp K 30 proved to be a good carrier for the preparation of solid dispersion of poorly water-soluble drugs.

All the observations of pre-compression parameters and post-compression parameters of fast-dissolving tablets and conventional tablets were observed within the range. All observations of In vitro1 disintegration time of fast-dissolving tablets were less than 1 min which complies with standards. It can be concluded that formulation TS5 shows the highest drug release than formulation TS4 because the combination of two super disintegrants gives a synergistic effect on the disintegration of the tablet, as compared to individual use.

It can be concluded that formulation TS4 and TS5 shows highest drug release than conventional tablet formulation .TS5 shows very fast drug release , as compared to formulation TS4 and conventional tablet because , in formulation TS5,two superdisintegrats were used in same proportion[i.e.2.5 %+2.5 %].These two superdisintegrants were shown combined synergistic effects on drug release , and hence giving fast disintegration.

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