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Enhancement Of Solubility And Dissolution Characteristics Of Aceclofenac By Solid Dispersion Technique

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ABSTRACT:

The present study focuses on enhancing the solubility and dissolution characteristics of Aceclofenac, a Biopharmaceutical Classification System (BCS) Class II drug with poor aqueous solubility, using the solid dispersion technique. The study employs two methods: fusion and solvent evaporation, incorporating PEG 6000 and PVP K32 as hydrophilic carriers. Preformulation studies, including FTIR analysis, confirmed no significant drug-excipient interactions, ensuring compatibility. Solid dispersions were prepared and evaluated for micrometric properties, flowability, in vitro drug release, and stability.

Results: The results demonstrated a significant improvement in solubility and dissolution rates, particularly with the formulation ASDF3 (fusion method with PEG 6000), which exhibited superior dissolution characteristics compared to ASDS3 (solvent evaporation with PVP K32). Based on in vitro drug release studies, the solid dispersion method effectively improved the dissolution profile of Aceclofenac, highlighting its potential for enhancing the bioavailability of poorly soluble drugs. The findings suggest that polymer selection and preparation method significantly influence the drug's solubility and dissolution behaviour.

Keywords: Solubility, Aceclofenac, Solid Dispersion, and Rate of Dissolution

INTRODUCTION:

More than 40 percent of the drug coming from high through put screening are poorly soluble in water compounds with poor Solubility are increasingly posing challenges in the development of new drugs, since a large number of drugs coming directly from synthesis or from high throughput screening have a very poor solubility. Poor aqueous solubility is known to significantly limit therapeutic efficacy by causing a low rate of dissolution and, consequently, reduced gastrointestinal absorption.tract after oral administration hence comprising oral bioavaibility. The ability to increase aqueous solubility is thus a valuable aid to increase the efficacy for certain drugs [1].

The Biopharmaceutical Classification system divides drugs into four classes depending on in vitro and in vivo permeability data. Four classes of compound can be distinguished: I (high solubility, high permeability), II (low solubility, high permeability), III (high solubility, low permeability) and IV (low solubility and low permeability). [2]

Typical instances for waiving bioequivalence studies are class I drugs. In the selection process, new chemical compound with low aqueous solubility and low permeability are preferably filtered out since they might pose problems during pharmaceutical development. Oral drug absorption is limited by Class II drug dissolution/solubility and Class III drug permeability. It is clear that class II medicines' poor dissolution capacity limits their total rate and extent of absorption more than their gut epithelial penetration capacity. Solid dispersion, surfactant solubilization, co-solvent use, particle size reduction, hydrotropic, and the use of water soluble derivatives or salts are some of the pharmaceutical techniques that can be used to increase the aqueous solubility of poorly soluble medications. Among all technique solid dispersion (SD), is the most efficient technique from the dispersion in carrier more specially define the system has the dispersion of the one or more active ingredient in an inert matrix at solid state perform by melting method, solvent evaporation method and melting solvent [3].

Since long, many investigators have studied SDs of poorly water-soluble drugs with various pharmacologically inert carriers to increase the dissolution and oral absorption of poorly water-soluble drugs, however, only a few systems are useful commercially [4].

Due to its higher stability, smaller mass, precise dosage, and ease of production, oral drug delivery is the most straightforward and straightforward method of drug administration. Among the solid dosage forms, they offer many advantages over other types of oral dosage forms. As a result, the majority of the novel chemical compounds being developed today are meant to be employed as solid dosage forms that, when taken orally, result in an efficient, repeatable in vivo plasma concentration. The majority of novel chemical entities are actually poorly soluble medications that are not well absorbed when taken orally, which can detract from the drug's natural effectiveness. There are several factors that can restrict the absorption of drugs from the gastrointestinal tract; the drug molecule's poor aqueous solubility and low membrane permeability are the most significant contributing factors.

Before an active substance to pass through the GI tract's membranes and enter the systemic circulation, it must first dissolve in the stomach and/or intestinal fluids. Thus, two fields of pharmaceutical study are concerned with increasing oral bioavailability Some active substances include improving the permeability and solubility of medications that are poorly soluble in water as well as their rate of dissolution. Developing methods to increase a drug's water solubility is one of the pharmaceutical industry's biggest current challenges. For oral drug bioavailability, drug release is an essential and limiting step, especially for drugs with high permeability and poor gastrointestinal solubility. It is feasible to increase these medications' bioavailability and lessen their adverse effects by enhancing their drug release profile. One of the best strategic methods for enhancing the release of poorly soluble medications is the use of solid dispersions. Solid dispersion can be defined as a molecular mixture of poorly water-soluble drugs in hydrophilic carriers, which present the drug release profile that is driven by the polymer properties.[5]

The matrix can be either crystalline or amorphous. Upon exposure to aqueous media, the carrier in the solid dispersions product dissolves, releasing the drug as fine colloidal particles with an increased surface area that produces a higher dissolution rate and improved bioavailability. The improvement of the dissolution of drugs from solid dispersions is based mainly on three different mechanisms: the reduction in particle size and increased surface area, the wettability of the drug, which is improved by direct contact with the hydrophilic matrix, and the conversion of the crystalline state to the more soluble amorphous state [6].

Various methods can be used to prepare solid dispersions, including solvent casting, kneading, co-precipitation, melting, co-grinding, gel entrapment, spray drying, melt extrusion, lyophilization and dropping method solution [7]

MATERIALS:

Aceclofenac was purchased from India Mart. PEG 6000 and PVP K32 were also purchased from India Mart. All reagents were of analytical grade All experiments were conducted using double distilled water.

METHODS:

A) PREFORMULATION STUDIES:

Drug-Excipient compatibility

In order to confirm no interaction happened between the drug substances and polymers, characterization of drugs and polymers and physical mixture of respective drug polymers were carried out by using Fourier Transform Infrared Spectroscopy (FTIR). [8]

Fourier Transform Infrared Spectroscopy (FTIR)

The test samples were dispersed in potassium bromate powder and analysed. FTIR spectrophotometer type FTIR 8400S Shimadzu, Japan was used to obtain FTIR spectra by diffuse reflectance. FTIR spectra were utilized to study compatibility between the drug and polymer. The positions of FTIR bands of important functional groups of drugs were identified and were cross checked with FTIR spectra of drug with excipients in 1:0.5,1:1.5,1:2.5 ratio.[9]

B) PREPARATION OF ACECLOFENAC SOLID DISPERSIONS:

Solvent Evaporation Method

The calculated amount of Aceclofenac and the employed polymer PVP K-32 of ratios 1:0.5, 1:1.5, 1:2.5, are weighed and mixed together in a porcelain dish. Three different formulae were prepared by the solvent evaporation method. The mixture was dissolved in small amount of methanol. Then the solvent was evaporated in oven at temperature 50°C until complete evaporation. The solid dispersions that were prepared underwent pulverization in a mortar and subsequent sieving.The fraction of the powder that passed through 45µm was stored in a desiccator and utilized for further study.[10]

Table No.1 Composition of Different Solid Dispersions of Aceclofenac prepared by Solvent Evaporation Method

	ASDS1	ASDS2	ASDS3
DRUG	1 %	1%	1 %
PVP K32	0.5%	1.5%	2.5%
Ratio:(Drug: Polymer)	**1:0.5**	**1:1.5**	**1:2.5**

Fusion Method

Solid dispersions were prepared by melting the accurately weighed amount of PEG 6000 in a water bath and drug were dispersed in a molten solution, & cooling immediately on ice bath with continuous stirring to dry mass. The dry mass was crushed and pulverized and stored. The drug-carrier ratio was used as 1:0.5, 1:1.5, and 1:2.5.[11]

Table No.2: Composition of Different Solid Dispersions of Aceclofenac prepared by Fusion Method.

	ASDF1	ASDF2	ASDF3
DRUG	1 %	1%	1 %
PEG 6000	0.5%	1.5%	2.5%
Ratio:(Drug: Polymer)	**1:0.5**	**1:1.5**	**1:2.5**

C)EVALUATION OF SOLID DISPERSIONS:

Percentage of Yield

The raw materials, amount of drug, either PVP K32 or PEG 4000 and other process parameters, which are going to determine and affects the percentage of yield during the preparation of solid dispersion. The yield was computed by weighing the solid dispersions loaded with drug and finding out percentage of yield against the weight of raw materials, i.e., weight of polymers and drugs used. The formula to calculate the percentage of yield is given as follow as:

$$\textbf{Percentage of Yield (\%)} = \frac{\text{Weight of Solid Dispersion}}{\text{Weight of polymer and drug in formulation}} \times 100$$

Drug Content

Solid dispersions equivalent to 20 mg of furosemide was weighed and transferred to a 50 ml volumetric flask, separately from SDFE1 to SDFE8. SDFEs were dissolved in 10 ml of methanol. The final volume was made up to 50ml with either pH 1.2 buffer and filtered through 0.45 µm membrane filters.5 ml of the stock solution was pipetted out and further diluted to 50 ml with pH 1.2 buffer for the solid dispersion formulations from SDFE1 to SDFE8 to give a final concentration of 20 µg/ml solution. Drug content was estimated by spectrophotometer from the absorbance obtained at 274 nm for the pH 1.2 buffers. The drug content was calculated from the absorbance obtained with the help of the calibration curve.[12]

Solubility Studies for Solid Dispersion of Aceclofenac

In 3 different conical flask 500 mg of SDFE was weighed and transferred. 50 ml of water, pH 1.2 SGF and pH 7.4 SIF media were added to individual conical flask and closed well. All the three flasks were sonicated for one hour and finally filtered by using 0.45 Micron Whatman Filter Papers. The clear solutions were appropriately diluted with respective dissolution media and absorbance values were noted at 274 nm by UV spectrophotometer for SGF and SIF respectively.[13]

Micromeritics studies of solid dispersions

Different micrometrics parameters like tapped density, bulk density, flow property, Carr's Index and Hausner ratio were used to evaluate the solid dispersions.

Bulk Density

The bulk density for solid dispersions was assessed by dividing powder volume over the mass of the powder cm^3. 5 gm of solid dispersions was poured in 2ml graduated cylinder. The volume taken by the powder was calculated to determine bulk density. Bulk density was calculated by equation: [14-15]

$$B_d = W / V_P$$

Where, Bd = Bulk density; W = Weight of the sample (g); V_P = Volume of solid dispersions (cm^3).

Tapped Density

Tapped density was estimated by dividing bulk volume over the mass of the powder cm^3. 5 gm of solid dispersions were placed into a 10 ml measuring cylinder. At the beginning, powder volume was noted at initial and measuring cylinder was tapped mechanically for 50 times, later noted the volume after 50 taps. The tapped density of all solid dispersion formulations was computed by dividing weight of powders in gram at the end tapped volume in cm^3.Tapped density was computed by using equation: [14-15]

$$Td = W/ Vp$$

Where Td = Tapped density; W = Weight of the sample (g); Vp = Volume of solid dispersions (cm^3)

Carr's Index

It is a dimensionless parameter, which provides similar degree as the angle of repose to predict the flow property of a granules/ powder. By using compressibility index and Hausner's ratio flow characteristics of powder's were studied. The compressibility index is used as alternative measures of shape and size, bulk-density, surface area and moisture contents of material since all these properties could affect the compressibility index. The Carr's index is the ratio between differences among the tapped density and bulk density is to tapped density and the product with 100 will provide percentage of compressibility index. The Carr's index is computed using the formula as follows and the association between compressibility and flow property are shown in the following Table No.3. The averages of three readings were used to compute the compressibility index from each of the solid dispersion formulations. [14-15]

$$CI = (Td - Bd)/ Td \times 100$$

Where CI = Compressibility Index; Td = Tapped density; Bd = Bulk density

Relationship between percentage compressibility and flowability

Table No.3: Relationship between percentage compressibility and flowability

Compressibility Index (%)	Flow property	Hausner's Ratio
<10	Excellent	1.000-1.110
11-15	Good	1.120-1.180
16-20	Fair	1.190-1.250
21-25	Acceptable	1.260-1.340
26-31	Poor	1.350-1.450
32-37	Very poor	1.460-1.590
>38	Very -very poor	>1.600

Hausner's ratio

By using the following equation Hausner ratio was calculated for the solid dispersion. [14-15]

$$HR = Td/ Bd$$

Where, HR = Hausner ratio; Td = Tapped density; Bd = Bulk density

Angle of Repose

Angle of repose was used to estimate the flowability of powders through a fixed funnel method. A funnel with the end of the stem cut perpendicular to its axis of symmetry kept arranged over a graph paper of height which was placed on a flat horizontal surface. Solid dispersions of respective drugs were poured separately over the funnel till the tip of the conical part of the funnel reaches the end of the funnel. The height

of the powder (h) and radius (r) were later measured with standard scale. The angle of repose (θ) for samples was computed using the following formula.

$$\text{Angle of Repose } (\theta) = \arctan(h/r)$$

The measurement was done in triplicate and mean of the measurement was used to compute the angle of repose for each of the formulation. [16]

Table No.4: Relationship among Angle of Repose and Flowability

Angle of repose, ɵ (º)	Flowability
<25	Excellent
25-30	Good
30-40	Passible
>40	Very poor

In vitro drug release studies

The in vitro release of drug profile for the formulated solid dispersions were done in USP XXIII basket type dissolution tester, TDT-08L, with an auto sampler consisting of 900 ml of pH 1.2 buffer for 3 hours. Capsules filled with solid dispersions were placed in dissolution media with constant stirring at 100 rpm and 37° ± 0.5°C temperature was maintained at bath. An aliquot of 10 ml of dissolution media were removed at an interval of every 30 minutes and fresh dissolution media was replaced immediately after sampling. The removed samples were analysed for drug content by UV Visible spectroscopy. [16]

RESULT AND DISCUSSIONS

Percentage yield for solid dispersion of Aceclofenac

The value of the percentage yield of the 6 formulae of Aceclofenac solid dispersion prior to sieve was ranged from 96%, 97.6% ,99.71%, 98%, 97.3%, and 99.2% for ASDF1, ASDF2, ASDF3, ASDS1, ASDS2, and ASDS3 respectively of solid dispersion prepared with Aceclofenac. The result obtained were satisfactory and reproducible on repeating the preparations. The data represented in the table no:5

Table No.5: Production yield of the prepared Aceclofenac solid dispersion

Formula code	Production yield (%)	Formula code	Production yield (%)
Prepared by Fusion method (using PEG 6000 as polymer)		Prepared by solvent evaporation method (using Povidone as polymer)	
ASDF1	96.00%	ASDS1	98.00%
ASDF2	97.6%	ASDS2	97.3%
ASDF3	99.71%	ASDS3	99.2%

Fig.no:1: Prepared solid dispersions by two methods (fusion and solvent evaporation method) in three different ratios of 1:0.5, 1:1.5 and 1:2.5.

CALIBRATION CURVE:

Standard curve of Aceclofenac

Aceclofenac solution showed UV λ_{max} at 274 nm and its spectra is shown in Fig No: 2, Fig No: 3, and Fig No: 4 respectively. An analytical method was developed. The developed method obeyed the Beer-Lambert's law at the concentration ranged between 10 and 50 µg/ml with a correlation coefficient of 0.9997 and 0.9999 for Aceclofenac in simulated gastric fluid (pH 1.2) and simulated intestinal fluid (pH 7.4) respectively and showed good linearity in the selected concentration range.

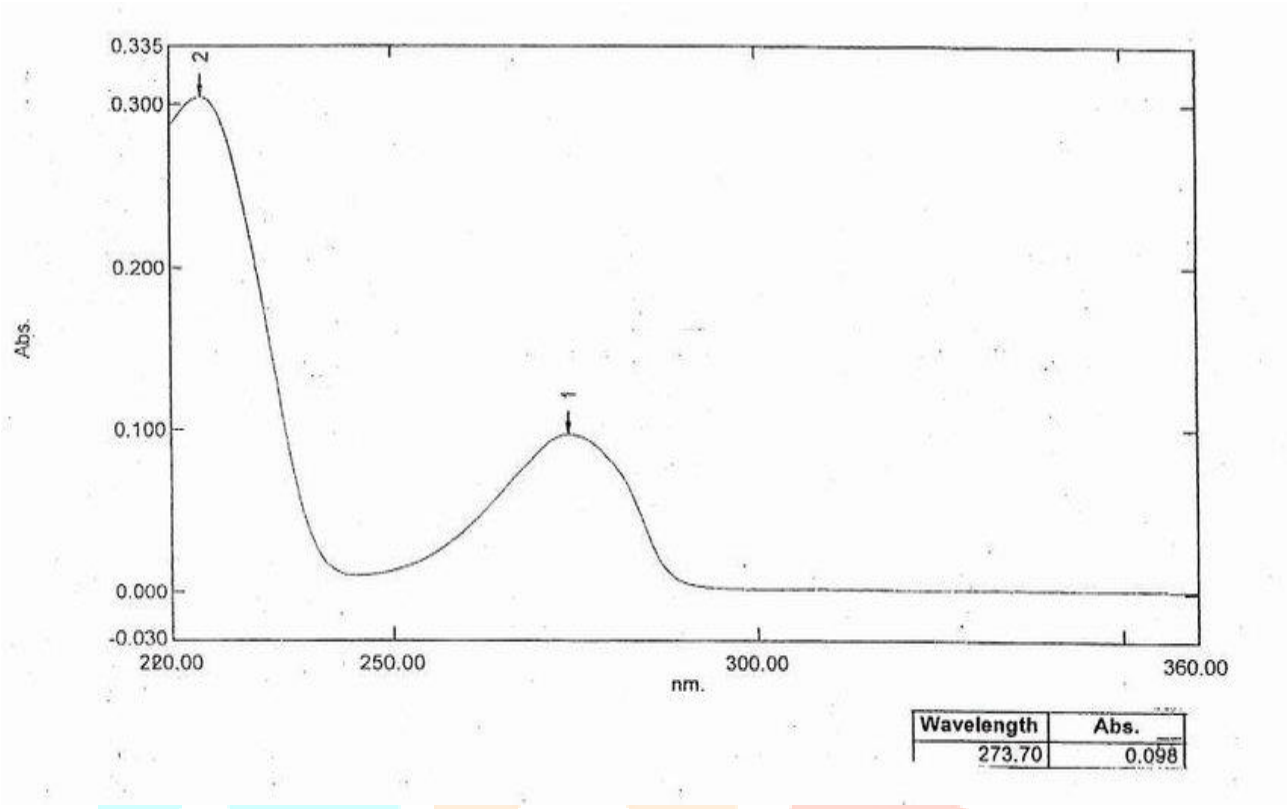


Fig.no.2: Spectra of Aceclofenac

Table No:6 Standard calibration curve of Aceclofenac in simulated gastric fluid (pH 1.2)

S. No	Concentration (µg/ml)	Absorbance at 274nm
1.	0	0.000
2.	10	0.124
3.	20	0.246
4.	30	0.368
5.	40	0.489
6.	50	0.601

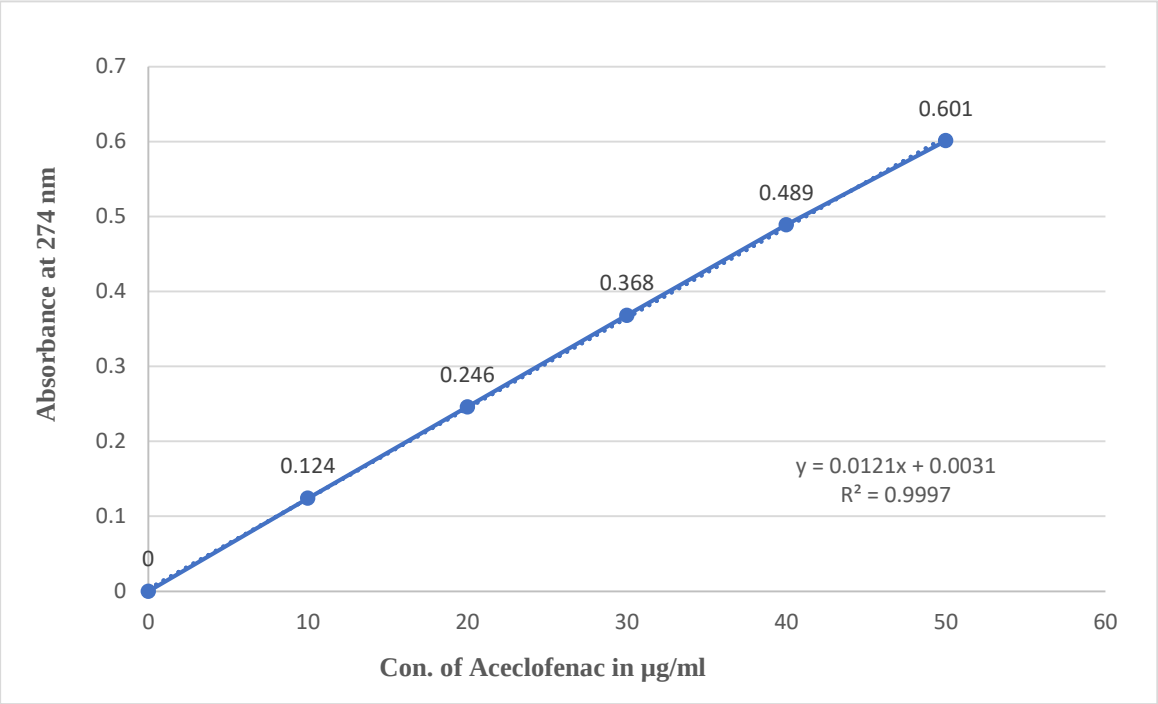


Fig.no.3: Calibration curve for Aceclofenac in simulated gastric fluid (pH1.2)

Table No:7 Standard calibration curve of Aceclofenac in simulated intestinal fluid (pH 7.4)

S. No	Concentration (µg/ml)	Absorbance at 274nm
1.	0	0.000
2.	10	0.118
3.	20	0.233
4.	30	0.359
5.	40	0.478
6.	50	0.599

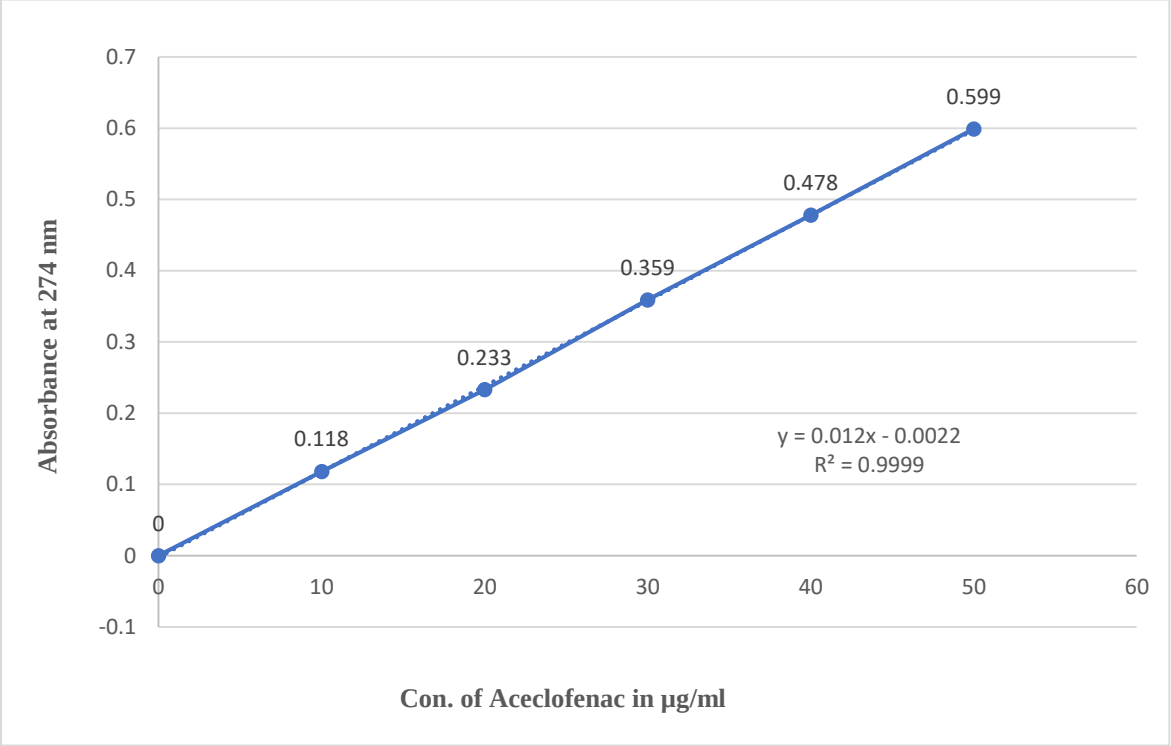
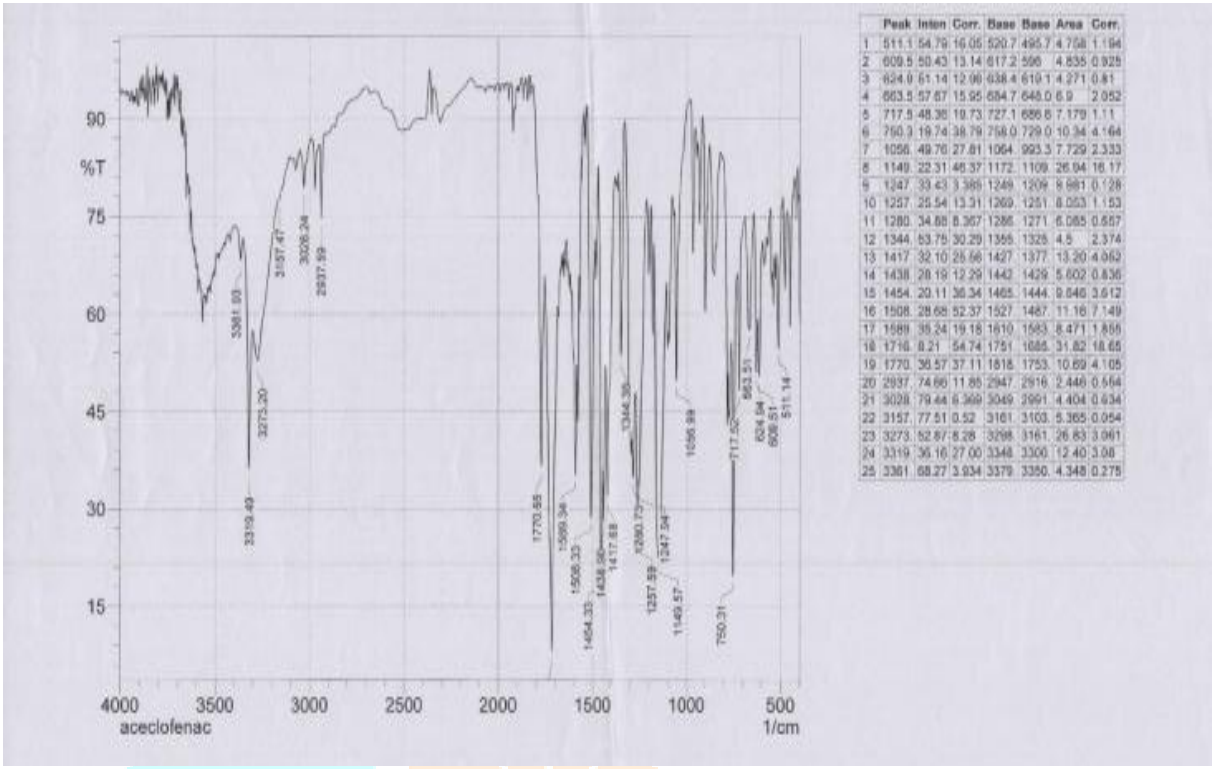


Fig.no.4: Calibration curve for Aceclofenac in simulated intestinal fluid (pH 7.4)

PREFORMULATION STUDY [Compatibility Study]

FTIR Spectra for Pure Aceclofenac and its solid dispersion

FTIR spectrum for drug and physical mixtures of Aceclofenac: PEG 6000 and Aceclofenac: PVP K32 was determined by KBr pellet method. Both samples were mixed with KBr pellets by applying hydrostatic press and spectra were obtained. Fig.No.5 to Fig.No.10 shows FTIR spectra of the drug and Fig.No.5 shows the standard drug of Aceclofenac, Fig.No.6 shows the spectrum of pure drug Aceclofenac, Fig.No.7 shows the spectrum of PEG 6000 polymer, Fig.No.8 shows the spectrum of Povidone K32 Polymer, Fig.No.9 shows the Spectrum of Pure Drug Aceclofenac and PEG 6000 Polymer and Fig.No.10 shows the Spectrum of Pure Drug Aceclofenac and Povidone K32 Polymer.



	Peak	Inten	Corr.	Base	Base	Area	Corr.
1	511.1	54.79	16.05	520.7	495.7	4.758	1.194
2	609.5	50.43	13.14	617.2	596	4.835	0.925
3	624.0	61.14	12.96	638.4	619.1	4.271	0.81
4	663.5	57.67	15.95	684.7	646.0	6.9	2.052
5	717.5	48.36	19.73	727.1	686.8	7.179	1.11
6	750.3	19.74	38.79	758.0	729.0	10.34	4.164
7	1056.	49.76	27.81	1064.	993.3	7.729	2.333
8	1149.	22.31	46.37	1172.	1109.	26.94	16.17
9	1247.	33.43	3.389	1249.	1209.	9.681	0.128
10	1257.	25.54	13.31	1269.	1251.	8.053	1.153
11	1280.	34.88	8.367	1286.	1271.	6.085	0.557
12	1344.	53.75	30.29	1355.	1325.	4.5	2.374
13	1417.	32.10	25.56	1427.	1377.	13.20	4.062
14	1438.	28.19	12.29	1442.	1429.	5.602	0.836
15	1454.	20.11	36.34	1465.	1444.	9.046	3.612
16	1508.	28.68	52.37	1527.	1487.	11.16	7.149
17	1589.	35.24	19.18	1610.	1583.	8.471	1.855
18	1716.	8.21	54.74	1751.	1686.	31.82	18.65
19	1770.	36.57	37.11	1818.	1753.	10.69	4.105
20	2937.	74.66	11.85	2947.	2916.	2.446	0.554
21	3028.	79.44	6.369	3049.	3991.	4.404	0.634
22	3157.	77.51	0.52	3161.	3103.	5.365	0.054
23	3273.	52.87	8.28	3298.	3161.	26.83	3.961
24	3319.	36.16	27.00	3348.	3300.	12.40	3.08
25	3381.	68.27	3.934	3379.	3350.	4.348	0.275

Fig.no.5: FTIR Spectrum for Standard Drug Aceclofenac

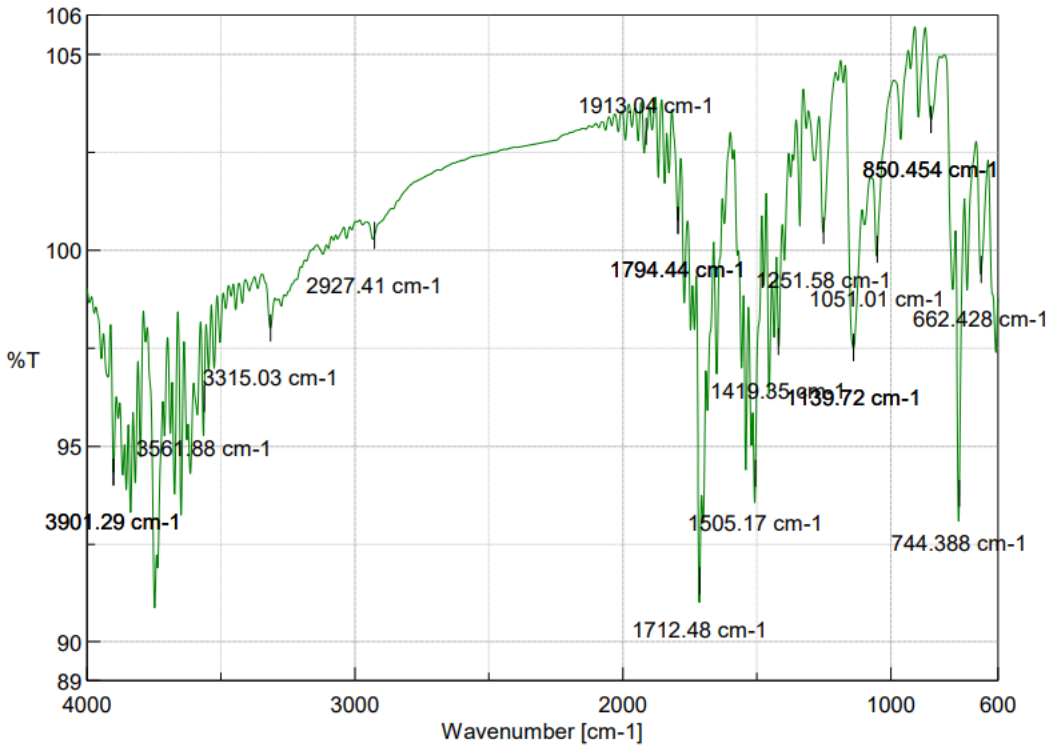


Fig.no.6: FTIR Spectrum for pure Drug Aceclofenac

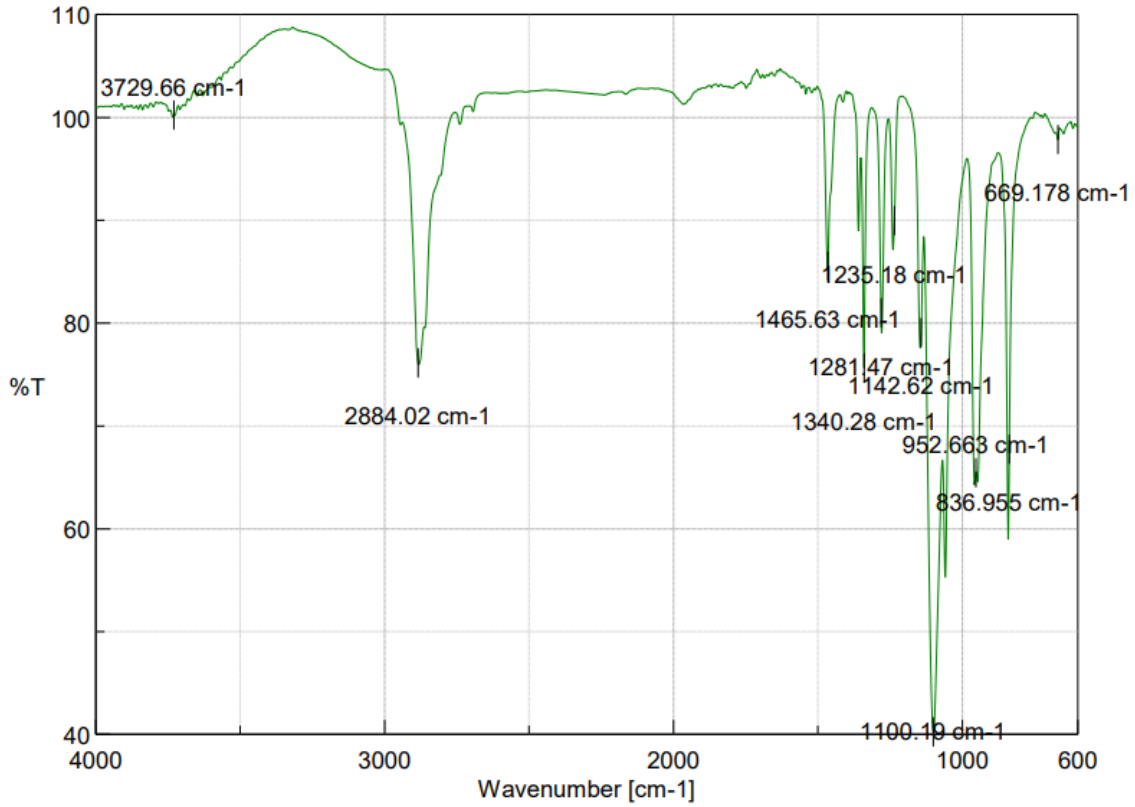


Fig.no.7: FTIR Spectrum for PEG 6000 Polymer

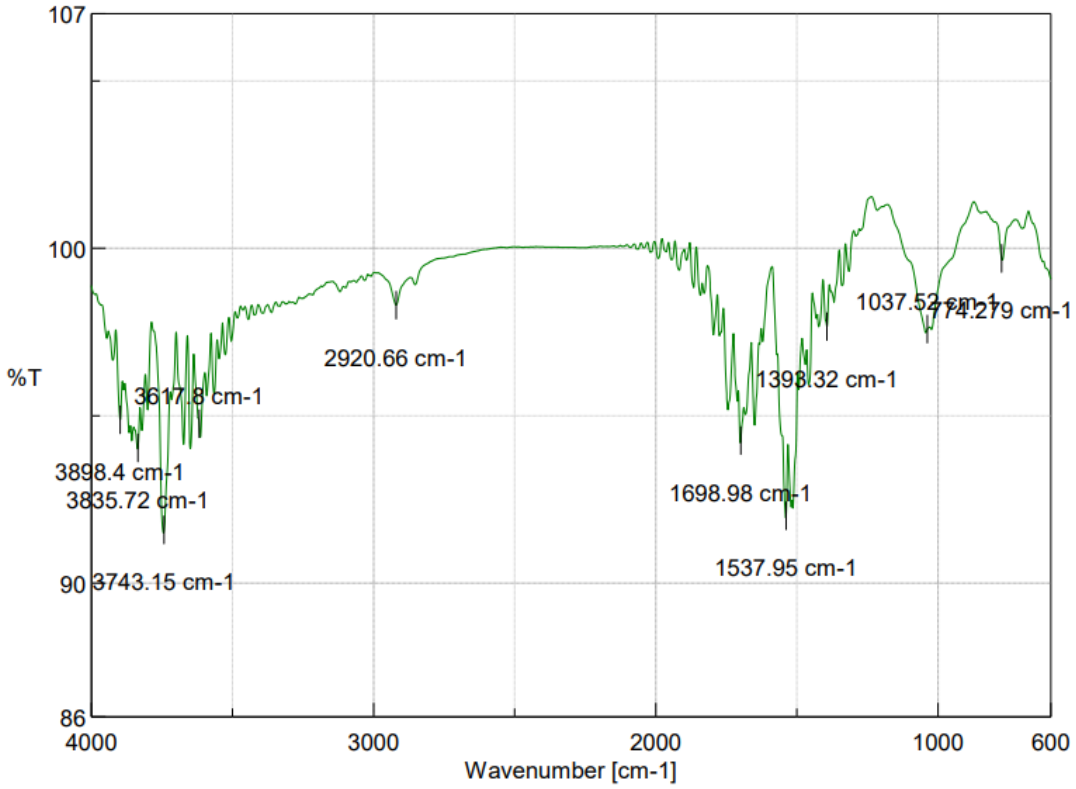


Fig.no.8: FTIR Spectrum for Povidone K32 Polymer

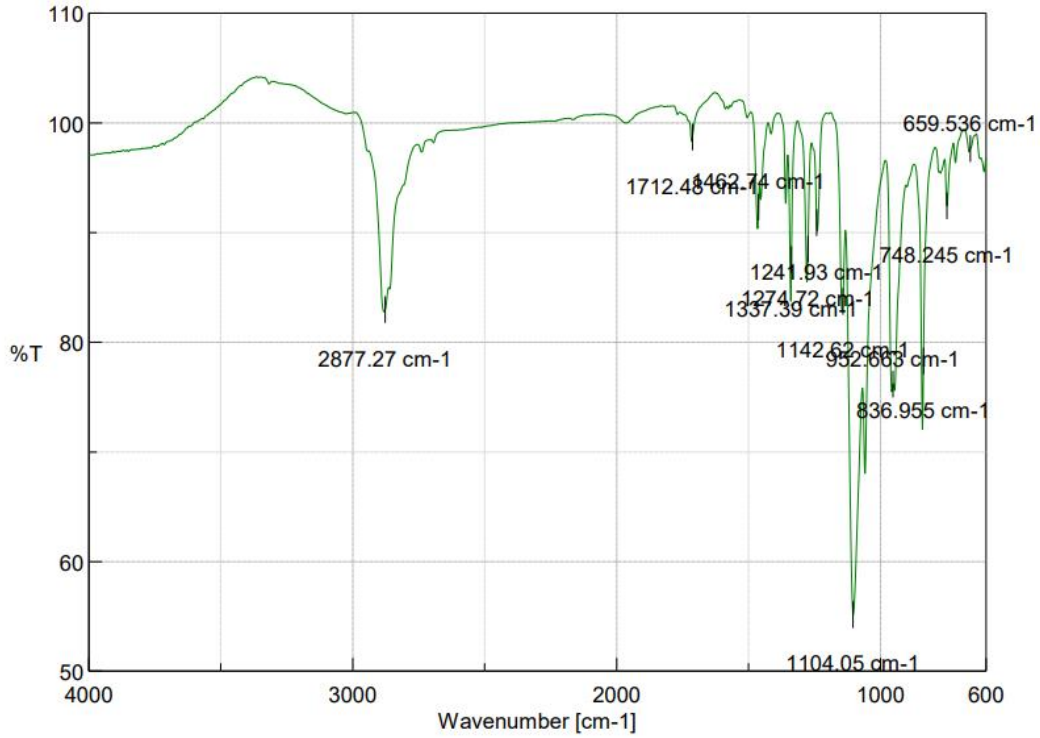


Fig.no.9: FTIR Spectrum for Pure drug Aceclofenac and PEG 6000 Polymer

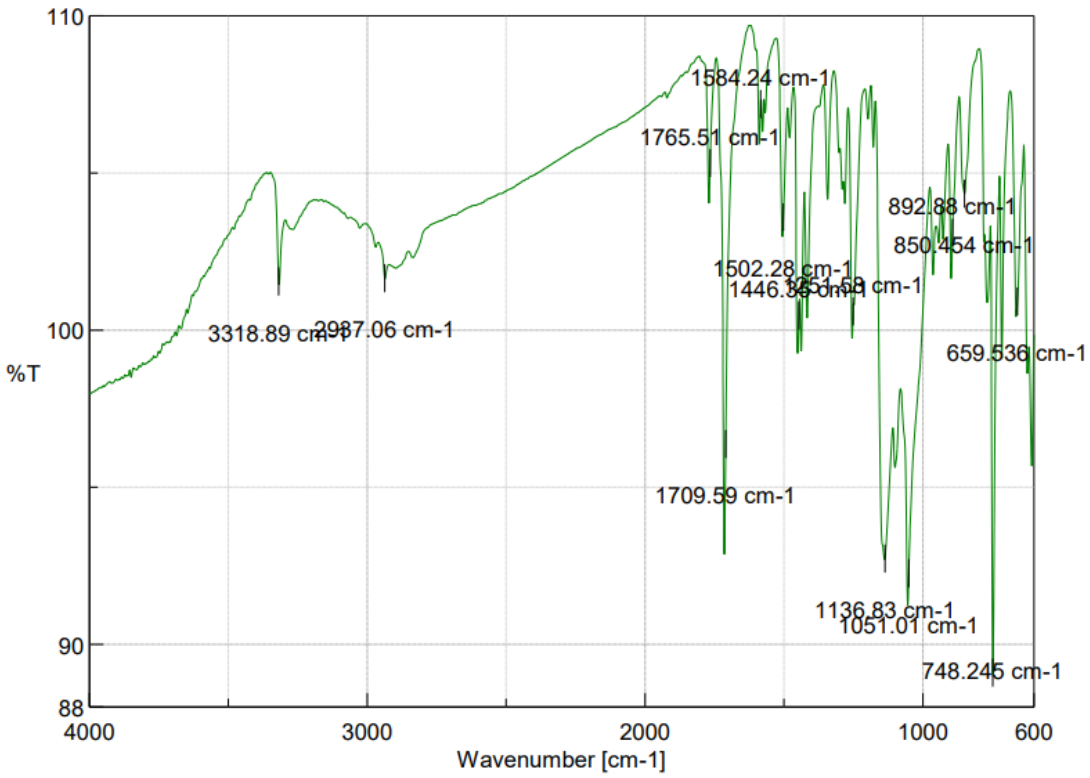


Fig.no.10: FTIR Spectrum for Pure drug Aceclofenac and Povidone K32 Polymer

IR spectra of pure drug Aceclofenac and with carriers like PEG 6000 as well as PVPK32 and have only characteristic peaks of the compounds. These studies showed that the drug is compatible between PEG 6000 and PVP K32. From the provided spectrum (from Fig.No.5 to 10) there were no significant alterations in the chemical integrity and functional group peaks for the pure drug Aceclofenac and its physical mixture in all the IR-spectra.

Phase Solubility Studies:

The results of solubility studies for the formulated solid dispersions of Aceclofenac in purified water, simulated gastric fluid at pH 1.2 and simulated intestinal fluid at pH 7.4 is given in Table No.8. The solubility of pure drug of Aceclofenac, ASDF1, ASDF2, ASDF3, ASDS1, ASDS2 and ASDS3 was found to be 1.273µg /ml, 25.02 µg / ml,31.33 µg / ml, 41.26µg / ml, 21.55µg / ml,31.55µg/ml and 41.07 µg/ml in purified water respectively, whereas in SGF for pure drug of Aceclofenac, ASDFI, ASDF2, ASDF3, ASDS1, ASDS2 and ASDS3 was found to be 1.501 µg / ml, 28.38µg / ml, 33.58µg / ml, 46.94µg /ml, 25.80µg /ml, 38.04and 46.05µg/ml respectively while in SIF for pure drug of Aceclofenac, ASDFI, ASDF2, ASDF3, ASDS1, ASDS2 and ASDS3 was found to be 2.002µg /ml, 30.18µg/ml, 35.49µg/ml, 49.68µg/ml, 26.24µg/ml, 40.24 µg/ml and 49.06µg/ml respectively.

Table No.8: Solubility Studies of Solid dispersions of Aceclofenac in different Media

	Amount of Drug Soluble (µg / ml)		
	Purified water	**SGF at pH 1.2**	**SIF at pH 7.4**
Pure Drug	1.273	1.501	2.002
ASDF1	25.02	28.38	30.18
ASDF2	31.33	33.58	35.49
ASDF3	41.26	46.94	49.68
ASDS1	21.55	25.80	26.24
ASDS2	35.62	38.04	40.24
ASDS3	41.07	46.05	49.06

The solubility studies data for pure drugs and formulated at purified water, simulated gastric medium (pH 1.2) and simulated intestinal medium (pH 7.4) was shown in the Table No.7. All the formulations, from ASDF1 to ASDS3 and pure drug have shown improved drug solubility when compared with respective pure drugs in all medium including solid dispersion. Among all the solid dispersion formulae, the formulations with optimal polymer concentrations i.e. ASDF3 (1:2.5), ASDS3 (1:2.5) have shown highest solubility in the respective medium. Additionally, improvement in solubility of Aceclofenac were affected by the polymer's concentration in solid dispersions formulae. As increase in the concentration of polymers, a majorly enhanced the effect of solubility was observed to an extent only on further increase in polymer concentration there is a drop in the solubility.

Estimation of Drug content for the Solid dispersions

The result of estimation of drug content in Aceclofenac solid dispersions is given in Table No.9.The percentage drug content of pure drug of Aceclofenac, ASDF1, ASDF2, ASDF3, ASDS1, ASDS2 and ASDS3 was found to be

Table.no.9: Percentage Drug content for the solid dispersions of Aceclofenac Prepared by PEG 6000 and PVP K32

Formulation code	Drug content (%)
Pure Drug	97.86
ASDF1	95.26
ASDF2	98.48
ASDF3	99.86
ASDS1	94.89
ASDS2	97.65
ASDS3	99.69

Percentage of drug content was estimated for selected solid dispersion formulations, which were performed by using UV spectrophotometer. The absorbances were taken and Percentages of drug contents were calculated. Percentages of drug contents for all formulations were observed in the range from 94.89% to 99.86% for ASD, which were within the Pharmacopoeial limits and shown in Table No.8.

On the other hand, solid dispersion of all the formulae prepared with Povidone K32 and PEG 6000 by fusion and solvent evaporation techniques was also showed an improvement in drug release from the solid dispersions particularly from the ASDF3 (1:2.5), ASDS3 (1:2.5) prepared when compared with pure drug of Aceclofenac.

As increase in the concentration of polymers, a majorly enhanced the effect of drug release was observed to an extent only on further increase in polymer concentration there is a drop in the drug release from the solid dispersions. In higher concentrations of selected polymers (Povidone K32 and PEG 6000), there is significant increase in the amount of drug released. This could be because of the reality that Povidone K32 and PEG 6000 showed increased solubility in water that resulted in improved wettability and drug particles solubility as well as indirectly improved its dissolution.

Estimation of Micrometrics Properties

Flow Properties for the Solid Dispersions of Aceclofenac

The angle of repose for pure drug of Aceclofenac was found to be 41º whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 34°, 28° and 26º in the formulations ASDF1, ASDF2, and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using Povidone K32 as polymer was found to be 38°, 32°, and 29° in the formulation ASDS1, ASDS2, and ASDS3 respectively. The results of angle of repose of solid dispersions for Aceclofenac are given in Table No.10.

Table No. 10: Flow Properties for the Solid dispersions of Aceclofenac Prepared by PEG 6000 and Povidone K32

	Angle of repose(º)	Carr's index (%)
Pure Drug	41	21.48
ASDF1	34	20.48
ASDF2	28	24.00
ASDF3	26	12.67
ASDS1	38	19.09
ASDS2	32	13.07
ASDS3	29	28.98

The Carr's Index for pure drug of Aceclofenac was found to 21.48% whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 20.48%, 24.00%and 12.67%in the formulations ASDF1, ASDF2, and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using PVP K32 as polymer was found to be 19.09%, 13.07%, and 28.98% in the formulations respectively. The results of Carr's index of solid dispersion for Aceclofenac are given in Table No:9.

Flowability of pure drugs of Aceclofenac and its solid dispersion were assessed by estimation of angle of repose and Carr's Index (CI) Flowability parameters of the pure Aceclofenac powered and all formulated solid dispersion are listed. Table No:9. represents the data an Flowability properties in term of Angle of repose and Carr's Index were much increased when compared with pure drugs powder, which might not pass through the funnel during the angle of repose. The poor flow of Pure drug might be because of the asymmetrical shape and greater fitness of the powder that was posed difficulties in the consistent flow from the funnel All the results found to be within the official Pharmacopoeial range. From the preformulation studies, it is clear that the Aceclofenac solid dispersions satisfied the official requirements for filling of capsule and from the physio mechanical characters showed perfect that all the capsules fulfilled official requirements of capsules. The results of angle of repose (values were between 20 and 28 for the ASDF3, ASDS3) and carr's index shows an excellent flow property for the formulated solid dispersions.

Physical Properties for the Solid Dispersions of Aceclofenac

The bulk density for pure drug of Aceclofenac was found to be 0.52g/ml whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 0.66g /ml, 0.62g/ml and 0.50g/ml in the formulations ASDF1, ASDF2, and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using PVP K32 as polymer was found to be 0.60g/ml, 0.68g /ml and 0.75g/ml in the formulation ASDS1, ASDS2, and ASDS3 respectively. The results of bulk density of Solid dispersions for Aceclofenac are given in Table No:11.

Table No.11: Physical properties for the solid dispersion of Aceclofenac prepared by PEG6000 and PVP K32

	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's Ratio
Pure Drug	**0.52**	**0.67**	**1.28**
ASDF1	0.66	0.83	1.25
ASDF2	0.62	0.71	1.14
ASDF3	0.50	0.62	1.24
ASDS1	0.55	0.60	1.09
ASDS2	0.52	0.68	1.30
ASDS3	0.63	0.75	1.19

The tapped density for pure drug of Aceclofenac was found to 0.67 g/ml whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 0.83g/ml, 0.71g/ml, and 0.62g/ml in the formulations ASDFI, ASDF2, and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using PVP K32 as polymer was found to be 0.60g/ml, 0.68g/ml, and 0.75g/ml in the formulations ASDS1, ASDS2, and ASDS3 respectively. The results of tapped density of solid dispersions for Aceclofenac are given in Table No.10.

The Hausner's ratio for pure drug of Aceclofenac was found to 1.25 whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 1.25, 1.14, and 1.24 in the formulations ASDF1, ASDF2, and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using PVP K32 as polymer was found to be 1.09, 1.30, and 1.19 in the formulations ASDS1, ASDS2, and ASDS3 respectively. The results of Hausner's ratio of solid dispersions for Aceclofenac are given in Table No.10.

From the results of bulk density, it is inferred, which powders is loosely packed and further bulk density values were utilized for Carr's Index and Hausner's ratio calculation. The Hausner's ratio shows that the prepared solid dispersions possess very good flowability. All the prefilling parameters were within the acceptable limits. The above values of pre filling characters showed that the prepared granules are having good flow and micromeritic properties.

In Vitro Dissolution Release Profile for Solid Dispersions

In Vitro Dissolution Profile Study for Pure Drug Aceclofenac and its Solid Dispersions

The in vitro dissolution profiles for pure drug of Aceclofenac was found to be 41.55% whereas for the solid dispersions prepared by fusion method using PEG 6000 as polymer was found to be 88.53%, 98.54%, 99.89% and 91.25% in the formulations ASDF1, ASDF2 and ASDF3 respectively. But for solid dispersions prepared by solvent evaporation using PVP K32 as polymer was found to be 95.25%, 98.55%, 99.24% and 95.85% in the formulations ASDS1, ASDS2 and ASDS3 respectively. The results of in vitro dissolution profiles of solid dispersions for Aceclofenac are given in Table No. 12.

Table No.12: Cumulative percentage Durg release of Aceclofenac Pure Durg and Solid Dispersion

Time (Min)	Pure Drug	ASDF1	ASDF2	ASDF3	ASDS1	ASDS2	ASDS3
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**
5	**1.57**	**15.63**	**27.34**	**38.56**	**16.35**	**48.51**	**66.52**
10	**4.73**	**36.52**	**44.03**	**53.22**	**37.32**	**60.50**	**77.321**
15	**10.87**	**51.66**	**57.27**	**66.21**	**55.02**	**70.20**	**82.59**
20	**15.52**	**68.59**	**73.01**	**74.62**	**67.41**	**77.4**	**90.52**
30	**24.56**	**79.86**	**87.07**	**88.22**	**74.20**	**86.72**	**93.54**
45	**32.45**	**82.14**	**90.34**	**95.46**	**82.55**	**89.32**	**96.57**
60	**38.62**	**84.46**	**96.52**	**97.04**	**88.02**	**92.12**	**97.56**
90	**42.65**	**88.35**	**98.52**	**99.87**	**92.20**	**96.25**	**99.72**

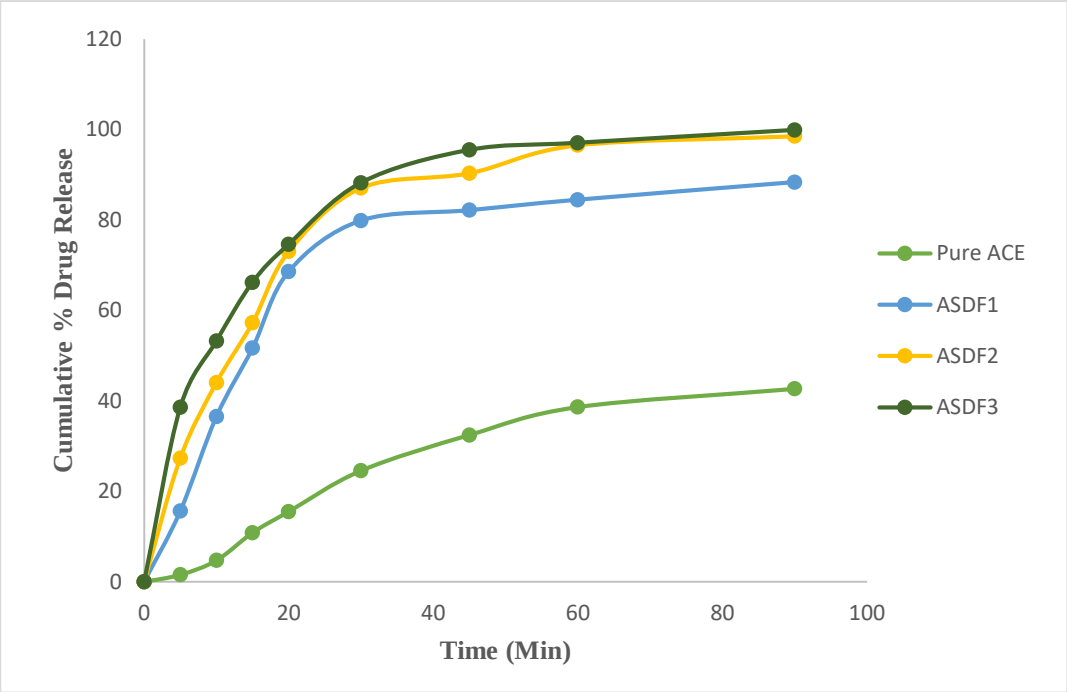


Fig.no.11: Cumulative percentage Durg release of Aceclofenac Pure Durg and Solid Dispersions prepared by Fusion Method

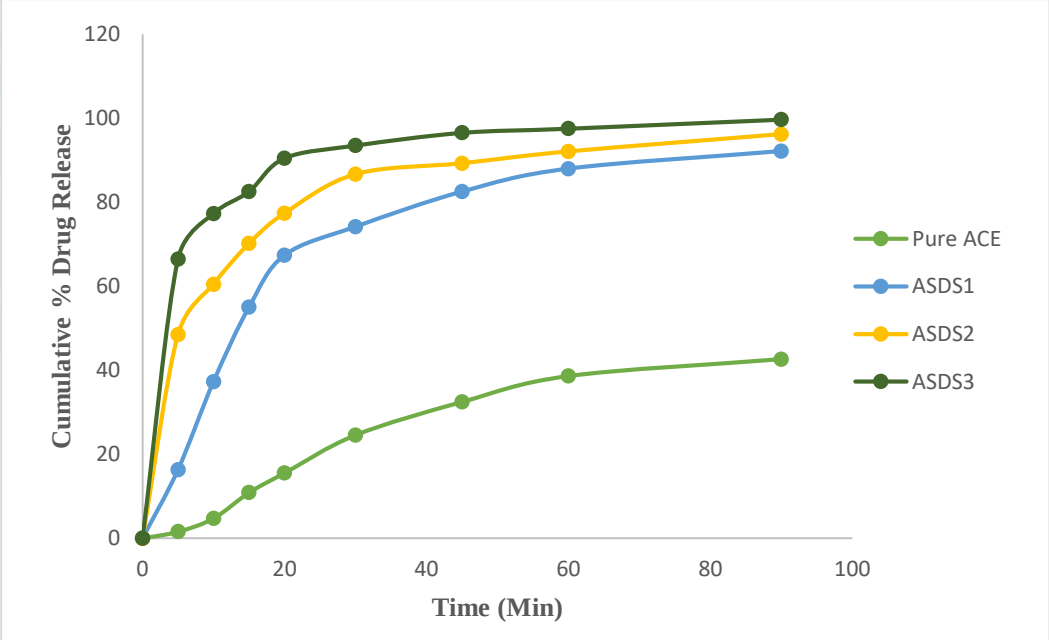


Fig.no.12: Cumulative percentage Durg release of Aceclofenac Pure Durg and Solid Dispersions prepared by Solvent evaporation method

In vitro drug release profiles of solid dispersions of Aceclofenac were prepared with various drug: polymer ratios as well as treated and pure drugs at pH 1.2 is presented in Table No. 11 and the same are depicted in the Fig. No. 11 and Fig. No. 12, respectively. Dissolution release rate of all solid dispersions prepared with three drugs were improved significantly when compared with the pure drugs Aceclofenac, which may be due to of increased hydrophilicity of the polymers. In solid dispersions, drug release profile was improved as a result of increase in polymer concentration up to ratio of 1:0.5; 1:1.5 and 1:2.5 for the Aceclofenac for the solid dispersion prepared by both fusion and solvent evaporation techniques. But

ASDF3 and ASDS3, have shown the maximum release profile at the drug polymer ratio of 1:2.5 and 1:2.5 respectively. Solid dispersions prepared by PEG 6000 with ratios of 1:2.5 and 1:2.5 have shown an improved dissolution profile when compared with the PVP K32 by the Solvent evaporation method. The percentage of drug released at pH 7.4 is evidently higher than the amount of drug release at pH 1.2 dissolution medium. This might be because of improved solubility of the weak acids of Aceclofenac may be due to higher ionization at elevated pH range.

SUMMARY AND CONCLUSION

The objective of the present study is to prepare solid dispersions of Aceclofenac with an air to increase in solubility and dissolution rate by employing various polyamide we medication is known as a diuretic (like a "water pill"). It promotes the production of urine, which aids your body in eliminating excess water. All the three drugs are belonging to BCS class II drugs, i.e. poor solubility and dissolution rate and practically insoluble in water Solid Dispersions were prepared by using different polymers at various concentrations by fusion and solvent evaporation methods. They were assessed for micrometric properties, flowability properties, in vitro drug release and stability studies.

Preformulation study was carried out for Aceclofenac and polymers utilized used in the formulations and they observed to be compatible. Evaluations were performed by FTIR studies, which are interpreted and found to be no interactions between the ACE with PEG 6000 and PVP K32 and found to be compatible. Solid dispersions of Aceclofenac prepared by fusion and solvent evaporation methods employing PEG 6000 and PVP K32 i.e. ASDF3 and ASDS3 were exhibited greater solubility and dissolution rate when compared to pure drugs. The micrometrics parameters and flowability like angle of repose and Carr's index and bulk density, tapped density and compressibility index respectively were assessed and observed to be excellent flow characteristics and fair Hasuner's index. Evaluations of capsules were carried out and found to be within specified limits. Based on the in vitro drug release profiles of respective solid dispersions and their capsules it is concluded that solubility and dissolution rate of Aceclofenac is increased by using the PEG 6000 and PVP K32 polymers.

On comparing with the PEG 6000 and PVP K32 prepared by fusion and solvent evaporation for all the three drugs, ASDF3 is having high solubility and dissolution rate when compared with ASDS3. Hence, the solubility and dissolution rate differ from method to method and polymer to polymer used in the formulations.

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