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Research Article

Formulation Development and In-vitro Evaluation of Solid Dispersions of a Poorly Soluble Drug Aceclofenac

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ABSTRACT

Increasing the solubility of aceclofenac, a BCS class-II drug that is poorly soluble in water, was the aim of the study. Aceclofenac appears to be particularly well tolerated among NSAIDs, with a lower incidence of gastrointestinal adverse effects. For oral medications that are poorly soluble, the rate of dissolution often controls the rate of absorption. To improve the drug's solubility, solid dispersions were created using a range of methods, such as physical mixing, kneading, and solvent evaporation, using various carriers, PEG 4000, in ratios ranging from 1:1 to 1:5. The physicochemical characteristics of the prepared formulations were evaluated using in-vitro dissolution studies, X-ray diffraction (XRD), differential scanning calorimetry (DSC), and saturation solubility. The solvent evaporation method was used to optimize PEG 4000 in a 1:5 ratio based on the evaluation parameters. The direct compression method was then used to formulate the tablets. These tablets showed a higher in-vitro dissolution drug release of 99.62% in 30 minutes compared to 26.62% in 60 minutes for the pure drug, and 99.64±0.10% in 40 minutes for the marketed tablet (Xerodol). Consequently, it was found that the solubility, absorption rate, and bioavailability of aceclofenac are enhanced when PEG 4000 is used in solid dispersion using the solvent evaporation method.

KEYWORDS: Aceclofenac;NSAIDs; PEG 4000; Solid dispersion; Solvent evaporation.

INTRODUCTION

Aceclofenac is a widely prescribed non-steroidal anti-inflammatory drug (NSAID) belonging to the phenylacetic acid derivative class. It is primarily indicated for the management of pain and inflammation associated with osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Despite its therapeutic efficacy, the clinical utility of Aceclofenac is limited due to its poor aqueous solubility and low dissolution rate, which in turn results in variable oral bioavailability. According to the Biopharmaceutical Classification System (BCS), Aceclofenac is categorized as a Class II drug (low solubility, high permeability), where

dissolution is the rate-limiting step for absorption[1-3].

To overcome these solubility-related challenges, various formulation strategies have been explored, among which solid dispersion (SD) technology has gained significant attention. Solid dispersions involve the dispersion of a poorly water-soluble drug in a hydrophilic carrier matrix, generally using techniques such as solvent evaporation, fusion (melt method), spray drying, or hot-melt extrusion[4,5].

A wide range of hydrophilic carriers such as polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), hydroxypropyl methylcellulose (HPMC), and poloxamers are employed in the preparation of Aceclofenac solid dispersions. These carriers not only improve solubility but also provide physical stability to the amorphous form of the drug[6,7].

The development of Aceclofenac solid dispersions has shown promising improvements in dissolution rate, bioavailability, and onset of therapeutic action, which may ultimately reduce dose variability and enhance patient compliance. Moreover, solid dispersion systems are relatively simple to prepare, cost-effective, and scalable for industrial production, making them a practical solution for the formulation challenges associated with Aceclofenac.

Materials and Methods

Materials

Aceclofenac was obtained as gift sample from Themis Medicare Pvt Ltd, PEG 6000, PVC, MCC, Magnesium stearate from SD fine chemicals Ltd., Mumbai, Methanol Rankem, Xerodol® Ipca Laboratories Ltd and Talcum powder Accord labs Ltd. Spectrophotometer UV 1800, Shimadzu, FTIR Bruker Alpha, Germany ALPHA II.

Methods

Preformulation study

a. Determination of melting point

The precision melting point equipment was used to determine the melting points of aceclofenac.

b. Analytical method validation of aceclofenac

The aceclofenac stock solution was prepared by dissolving 50 mg of aceclofenac in methanol and adding methanol to equalize the volume. Standard dilutions of various concentrations were prepared by transferring stock solutions to 10 mL volumetric flasks. The λmax of aceclofenac was determined by measuring 10 mg of aceclofenac and adding it to a 100 mL volumetric flask with 50 mL of methanol. A calibration curve was constructed by creating methanolic solutions of various concentrations. The method was validated for linearity, range, limit of detection, and limit of quantitation. The absorption maximum (λmax) of 271 nm was observed[8-10].

c. Drug-excipientscompatibilitystudies

d. Drug-excipientscompatibilitystudies

The study used isothermal stress testing to study drug-excipient compatibility. 10 mg of PEG 4000 and pure aceclofenac were weighed and filled into glass jars. Ultra-pure water was added to each vial, and the vials were sealed and kept for four weeks. Organoleptic characteristics were assessed to detect physical instability, and temperature was traced using a Differential Scanning Calorimeter (DSC) from 30 - 300 °C at the rate of 30 °C/min, with a one-minute hold time at 30 °C in order to detect the chemical instability (Perkin Elmer, Japan)[11-13].

Preparation of solid dispersion

The physical mixture method (PM) and kneading method (KM) are methods used to create solid dispersions of drugs with different carriers. The blending method creates mixtures with different drug to carrier ratios, while the kneading method uses rotary flash evaporators and solvent evaporation to create dispersions[14,15].

Characterizationofsoliddispersions

a. Drug assay

Distilled water was used to test the solid dispersions that had been prepared. The drug was dissolved by adding 20 mL of methanol to a 100 mL volumetric flask that contained 100 mg of the drug in precisely weighed amounts of solid dispersions. After that, the flask was shaken for 20 min. The volume was adjusted to 100 mL using a phosphate buffer with a pH of 6.8. A 1 mLaliquot of the previously mentioned solutions was taken after the dispersions were filtered, and it was diluted with 6.8 pH phosphate buffer to make 10 mL. The absorbance of these solutions was measured at 271 nm using a UV spectrophotometer in relation to the blank, which was a phosphate buffer with a pH of 6.8. The percentage of the assay was calculated[16,17].

b. Solubilitystudies

An excess of pure aceclofenac drug and prepared solid dispersions were added to screw capped bottles containing distilled water. Bottles are shaken mechanically at 26 °C for 24 hours and aliquots are withdrawn, filtered and assayed for drug content at 271 nm using UV-Spectrophotometer[18,19].

c. In-vitroDissolutionstudyof aceclofenacsolid dispersion

Dissolution studies were performed with solid dispersions prepared by different methods and also compared with the pure aceclofenac drug. Dissolution apparatus USP type II (paddle) with revolutions per min (speed) 100 RPM was used with conditions 37 ± 0.5°C temperature, dissolution media 6.8 pH phosphate buffer volume of dissolution media 900 ml, aliquot withdrawn 5 ml Aliquot replaced 5 ml of the fresh buffer solution. Sampling was done at 10 min time intervals up to an hour[20,21].

d. Pre compression parameters of the powder blend

i. Angle of repose (Ø)

After precisely weighing 100 grams of the mixture, it was carefully poured through a funnel

with the tip fastened 2.5 cm above the graph paper that was set out on a horizontal surface. The mixture was poured until the conical pile's apex barely touched the funnel's tip. Table 4.8 illustrates the relationship between the powder's flow characteristics and angle of repose. Equation 1 provides the following formula for calculating angle of repose.

$$\emptyset = Tan - 1\left(\frac{h}{r}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots ii$$

Where,Ø =angleofrepose, r=radiusof thepile, h=heightof the pile. The reference values for corresponding angle of repose and type of flow is excellent (25-30), good (31-35), fair (36-40), passable (41-45), poor (46-55), very poor (56-65) and extremely poor (> 66).

ii. Bulk density

Apparent bulk density (*b) was determined by pouring the blend into a graduated cylinder. The bulk volume (V*) and weight of the powder (M) was determined. The bulk densitywas calculated using the formula given in Equation iii.

$$* b = \frac{M}{V} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots iii$$

iii. Tappeddensity

The measuring cylinder containing a known mass of blend was tapped for a fixed time (around 250). The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (*t) was calculated using the formula given in Equation iv.

$$* t = \frac{M}{Vt} \ldots\ldots\ldots\ldots\ldots\ldots iv$$

iv. Carr'sindex

The simplest way for measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibilityindex (C.I) which is calculated using the formula given in Equation v. The correlation between the compressibility index and flow properties of powder are as excellent (< 10), good (11-15), fair (16-20s), passable (21-25), poor (26-31), very poor (32-37) and extremely poor (>38).

$$C.I\ (\%) = \frac{(tapped\ density\ - Bulk\ density) \times 100}{Tapped\ density} \ldots\ldots\ldots\ldots$$

v. Hausner'sratio

Hausner's ratio is an indirect index of ease of powder flow. It was calculated by the using the formula given in Equation vi.The correlation between the Hausner's ratio and flow properties of powder are shown in the Table 4.10.

Hausner'sratio= *t/*d----------*vi*

Where*t=tappeddensityand *d=bulk density. Corresponding values for Hausner's ratio for different types of flow is excellent (1.00-1.11), good (1.12-1.18), fair (1.19-1.25), passable (1.26-1.34), poor (1.35-1.45), very poor (1.46-1.59) and extremely poor (> 1.60)[22-25].

Preparation of aceclofenac tablets by direct compression method

Tablets were made from the solvent evaporation method's optimized solid dispersion, which had a 1:5 ratio and contained the drug and poloxamer 407. Each of the additional tablet excipients listed in Table 1, including the diluent (mannitol), binder (PVP), sweetener (sodium saccharin), lubricants & glidants (talc and magnesium stearate), and direct compressive vehicle (MCC), were individually triturated in a mortar and run through a #60 sieve. After that, the necessary amounts of each ingredient were weighed for a batch size of fifty tablets and combined evenly in a mortar. Lastly, talc and magnesium stearate were added as lubricants. Using 11.1 mm flat face surface punches on a Rimek-1 rotary tablet machine, this evenly blended mixture was compressed using the direct compression method to create tablets with 100 mg of medication. Total weight of tablet was kept 650 mg[26-28].

Table 1: Formulations for SDSEM5 tablet

Nameof the ingredient	Quantity(mg)
Drug(equivalent amount of solid dispersion) (mg)	598
Microcrystallinecellulose (2%)	13
PVP(2%)	13
Mg.stearate(2%)	13
Talc (2%)	13
TotalWt. (mg)	**650**

Note:*SDSEM5 Formulations oftablets containing1:5 ofdrugand PEG 6000*

Evaluation of aceclofenac tablets

The prepared tablets can be evaluated for following parameters.

a. Weight variation

Twenty tablets were chosen at random, and their average weight was calculated. The percentage deviation from the average was then computed after each tablet was weighed separately. The weight variation limits listed in Table 4.12 [107]. The permissible limits for weight variation with respect to average tablet weight is 10% (130 mg or less), 7.5% (More than 130 mg) and 5 % (More than 324 mg)

b. Thickness

Controlling the tablets' physical attributes, like their thickness and size, is crucial for both tablet uniformity and consumer acceptance. The die and punches used to make the tablets determine their diameter and punch size. A screw gauge is used to measure the tablet's thickness. The tablet's thickness and hardness are correlated. The thickness of tablets should be kept within a standard range of ± 5%. Controlling thickness is also necessary to make packaging easier. A screw gauge was used to measure each of the ten pre-weighed tablets' thickness in millimeters (mm). Both the standard deviation and the average thickness were reported.

c. Hardness

Tensile strength (Kg/cm2) is a measure of tablet strength. The force needed to compress a tablet

into pieces is known as the tablet crushing load. A tablet hardness tester (Monsanto hardness tester) was used to measure it. For every formulation batch, three tablets were randomly tested, and the average reading was recorded.

d. Friability

The Roche Friabilator (Electrolab, India) was used to assess the tablets' friability. This apparatus consists of a plastic chamber that is programmed to rotate at a speed of 25 rpm for four minutes, dropping the tablets six inches apart with each rotation. Twenty tablets that had been previously weighed were put in the friabilator and rotated 100 times. The tablets were reweighed after being cleaned with a gentle muslin cloth. Equation 6 provides the formula for the friability (% F).

$$\% \ F = (1 - W_0/W) \times 100 \quad \text{.....vii}$$

Where, W_0 is weightof thetabletsbeforethetestandW is theweight ofthetablets aftertest

e. Content Uniformity

Tablets are finely powdered and powder equivalent mg of drug is accurately weighed and transferred to 100 ml volumetric flasks containing solution of desired pH. The flask is shaken to mixthecontentsthoroughly.Thevolumeismadeupt othemarkwithsolutionandfiltered.Oneml of the filtrate is suitably diluted and drug content is estimated using a double beam UV-visible spectrophotometer. This procedure is repeated thrice and the average value is calculated.

f. Disintegrationtime

Disintegrationtimewasmeasuredusingadisintegrationapparatus.Forthispurpose,aglassbeaker wasfilledwith900mlofmediaat37°C±0.5°C.Thetablet wascarefullyputinthecenterofthe tablet assembly and the time for the tablet to completely disintegrate into fine particles was noted.

g. In-vitro drug release

In-vitrodrugreleaseofaceclofenactabletswasdetermined byusingUSPdissolutiontestapparatus II (Paddle type) (Electro lab TDT-08L) and compared with marketed tablets (Xerodol®). The conditions for dissolution test given below:

Absorbance of solution was checked by UV Spectrophotometer (UV 1800 double beam spectrophotometer) at a wavelength of 274.8 nm and drug release was determined from standard curve[29].

h. Acceleratedstabilitystudiesforaceclofenac tablets

The optimized formulation of aceclofenactablets was subjected to stability studies at 40°C±2°C/75%±2% RH for period of one month. Each tablet was individually wrapped in aluminumfoilandpackedin ambercoloredbottleandputatabovespecifiedcondit

ioninaheating humidity chamber for one month. The tablets were analyzed for the hardness, disintegration time, and drug content and *in-vitro* drug release[29].

RESULTS

Preformulation study of the drug aceclofenac

Preformulation studies are lab tests aimed at comprehending the physicochemical characteristics of the drug material and possible excipients that are carried out prior to the actual formulation process starting. The goal of these studies is to produce a stable, safe, and effective drug product by optimizing the formulation and manufacturing process.

Melting point determination

Melting point of the drug aceclofenac was recorded and complied with the literature. The melting point of aceclofenac was recorded as 147°C.

Solubility analysis of pure aceclofenac API

Solubility of the drug aceclofenac was found 0.0265±0.015 in comparison to reported value of 0.056 mg/mL (Table 2).

Table 2 Solubility of the pure aceclofenac API

S. No.	Drug	Solvent	Solubility (mg/mL ±SD)	Reported Value (mg/mL)
1	Aceclofenac	Distilled water	0.0265±0.015	0.056

Analytical method validation

Maximum absorbance took place at 271 nm in methanol. The calibration curve was subjected to least square regression analysis to get optical features tabulated in table 3.

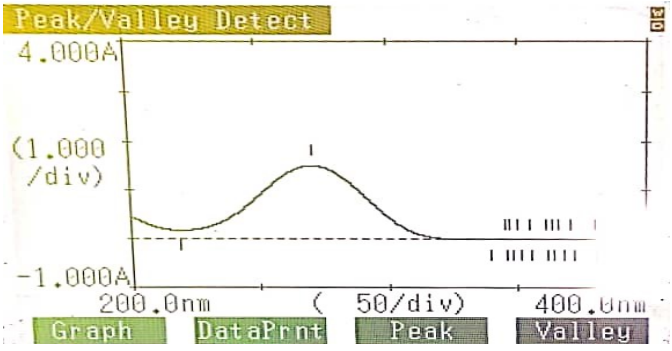

Figure 1: Scanning spectra of the drug aceclofenac in methanol for λmax determination

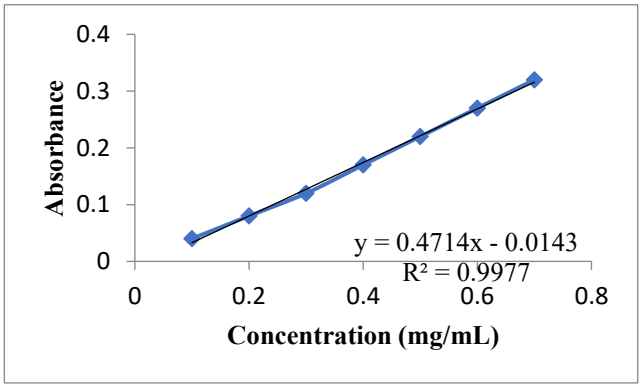

Figure 2: Calibration curve of the drug aceclofenac in methanol at 271 nm

Table 2: Data showing results of regression and optical features of the analytical method of aceclofenac

Parameters	Values
Linear dynamic range (µg/mL)	0.1-0.7
Regression equation	y = 0.4714x - 0.0143
Correlation coefficient (r)	R^2 = 0.9977
SE intercept	0.00451754
SD intercept	0.01195
LOD (µg/mL)	0.2431
LOQ (µg/mL)	1.0523
Variance of the calibration line	0.05153

4.1.4 Drug-excipientcompatibilitystudiesbyFTIR

FTIR analysis of the pure drug and polymer along were done to verify if there was any interaction between the pure drug and various excipients employed. The FTIR graphs of pure drug and various excipients were mixed and the blend was formulated into IR pellet and scanned using FTIR. The spectra shown in Figure 3, 4 results depicted in Table 3, 4.

Table 3: Interpretation of FTIR graph of pure drug aceclofenac

S. No	Region in cm-1	Type of vibration	Functional group present
1	3319.26	N-H Stretch	Amine
2	750.26	C-Hbend	Aromatic
3	1149.50	C=Cbend	Aromatic

Table 4: Interpretation of FTIR graph of aceclofenac and PEG 4000

S. No	Region in cm-1	Type of vibration	Functional group present
1	3319.26	N-H stretch	Amine
2	1716.53	C=Cbend	Aromatic
3	750.26	C-Hbend	Aromatic
4	1452.30	C=Cbend	Aromatic

From the above IR graphs the peaks representing the pure drug were found similar in formulation graph (ACP415SM) suggesting that there is no interaction and the pure drug is not altered functionally.

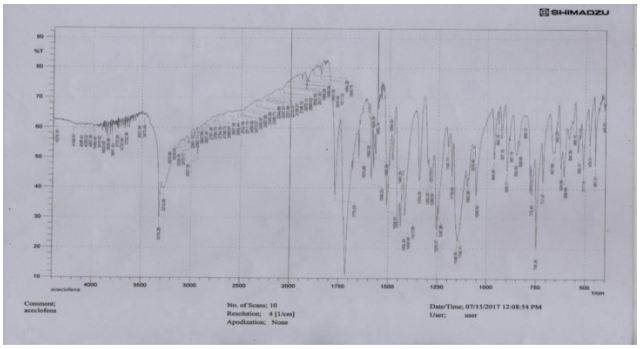

Figure 3: FTIR graph of aceclofenac (Pure drug)

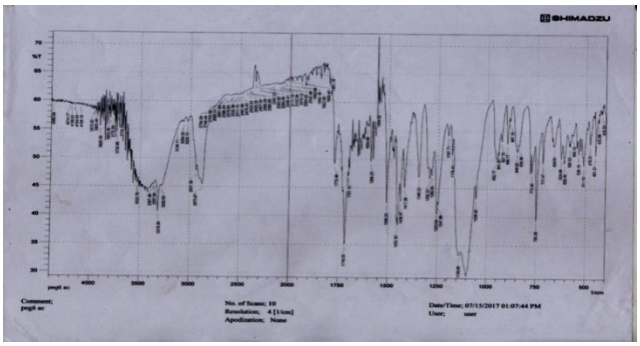

Figure 4: FTIR graph of aceclofenac and PEG 4000

7.1.5 ThermalanalysisbyDSC

DSC examined the characteristics of the solid aceclofenac dispersions made with PEG 4000 (SDSEM5). Melting point, and peak appearance was determined. Likewise, DSC was used to analyze the plain drug in the same way, noting the melting point and peak onset values. To compare the outcomes, the thermograms of the solid dispersions and the plain medication were superimposed. The pure drug's DSC revealed a distinct peak at 8.8.25 cal. SDSEM5's DSC revealed the drug's peak characteristics without any extra peaks. The drug and carrier did not interact, according to the DSC (Figures 5 and 6).

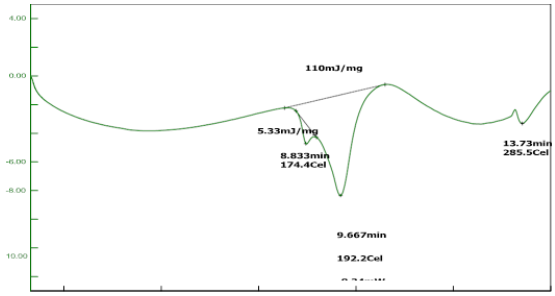

Figure 5: DSC graph of pure drug (aceclofenac)

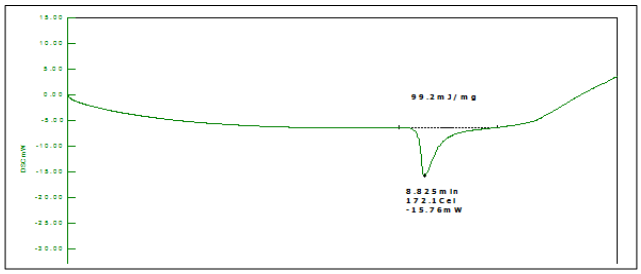

Figure 6: DSC graph of formulation SDSEM5

4.2 Preparation of aceclofenac solid dispersions

Solid dispersions of drug aceclofenac were prepared with PEG 6000 in varying proportions from 1:1 to 1:5 using different methods (physical mixture, kneading and solvent evaporation). Table 5 depicts the proportion of drug and polymer utilized for solid dispersion preparation using different methods and with varying proportions from 1:1 to 1:5.

Table5:FormulasofAceclofenacsoliddispersions(SDs)preparedbyphysicalmixtures

Method opted	Formulation code	Ratioof themixtureof drugandcarrier(D:C)	Weight ofthe drug (mg)	Weight ofthe carrier (mg)
Physical mixture	SDPMM1	1:1	100	100
	SDPMM2	1:2	100	200
	SDPMM3	1:3	100	300
	SDPMM4	1:4	100	400
	SDPMM5	1:5	100	500
Kneading method	SDKM1	1:1	100	100
	SDKM2	1:2	100	200
	SDKM3	1:3	100	300
	SDKM4	1:4	100	400
	SDKM5	1:5	100	500
Solvent evaporation	SDSEM1	1:1	100	100
	SDSEM2	1:2	100	200
	SDSEM3	1:3	100	300
	SDSEM4	1:4	100	400
	SDSME5	1:5	100	500

4.3 Evaluation of solid dispersions (SDs)

Solid dispersions were prepared by physical mixture; kneading and solvent evaporation methodswere evaluated for assay, solubility, dissolution studies and pre-compression parameters.

4.3.1Solubilityanalysis of solid dispersions

Solubilityof aceclofenac by physical mixture method, formulation SDPMM5 showed maximum solubility of 0.272±0.11 mg/ml. By kneading method, formulation SDKM5 showed 0.308±0.12 mg/ml. By solvent evaporation method, formulation SDSEM5 showed 0.331±0.006 mg/ml. It has been observed, as the concentration of carrier (PEG 4000) increased, the solubility was enhanced. Among the three different methods, solvent evaporation method showed maximum solubility of 0.331±0.006 mg/ml when compared with pure drug (0.0265 mg/ml). Formulation SDSEM5 showed maximum solubility in distilled water. Solubility studies of aceclofenac solid dispersions results showed in Table 6.

Table6:Solubilitystudiesofaceclofenacsolid dispersions

S. No.	Formulation code	Solubility (mg/ml ± SD)
1.	SDPMM1	0.228±0.09
2.	SDPMM2	0.236±0.08
3.	SDPMM3	0.246±0.10
4.	SDPMM4	0.253±0.11
5.	SDPMM5	0.266±0.13
6.	SDKM1	0.262±0.10
7.	SDKM2	0.277±0.18
8.	SDKM3	0.283±0.15
9.	SDKM4	0.292±0.14
10.	SDKM5	0.308±0.12
11	SDSEM1	0.298±0.009
12.	SDSEM2	0.302±0.012
13.	SDSEM3	0.311±0.011
14.	SDSEM4	0.316±0.010
15.	SDSEM5	0.320±0.008

4.3.2 Drug assay

The prepared solid dispersions complied with the requirements of assay. The result for assay for SDSEM was 99.14±13%. These percentage drug values indicated that the drug content is uniform in all the batches. Formulation SDSEM5 showed maximum assay value than other formulations.

4.3.3 Precompression parameters

Solid dispersions prepared by physical mixture method, kneading method and solvent evaporation method were evaluated for precompression parameters, mainly flow properties. Precompression parametersofthe aceclofenacpowderblend containingSDsbyphysical mixture,kneadingmethod and solvent evaporation method shown in Table 7, Table 8 and Table 9respectively.

The angle of repose of above physical mixture formulations ranged between 30.0±0.15 to 38.0±0.11 inferring fair flow property. Carr's index ranged from 1.98±0.06 to 16±0.01 inferring fairflowproperty.Hausner'sratioranged from1.01±0.05to1.19±0.18inferringfairflow property.

Table 7 Precompression parameters of the aceclofenac powder blend containing SDs by physical mixture

Formulation code	Angle of repose(Ø)	Bulk density gm/cm^3	Tapped density (gm/cm^3)	Hausner's ratio	Carr's index(%)	Assay (%)
SDPMM1	35.0±0.12	0.328±0.15	0.348±0.01	1.06±0.08	5.74±0.01	97.53±0.09
SDPMM2	33.0±0.11	0.331±0.01	0.351±0.12	1.06±0.10	5.69±0.09	98.67±0.12
SDPMM3	34.0±0.25	0.335±0.04	0.355±0.15	1.05±0.05	5.63±0.11	96.33±0.08
SDPMM4	32.0±0.01	0.341±0.04	0.357±0.01	1.04±0.11	4.48±0.14	97.58±0.11
SDPMM5	30.0±0.15	0.352±0.12	0.359±0.02	1.01±0.15	1.98±0.06	98.69±0.15

The angle of repose of above formulations ranged between 34.0±0.12 to 42.0±0.11inferring fair flow property. Carr's index ranged from 10±0.10 to 21±0.10 inferring fair flow property.Hausner's ratio ranged from 0.88±0.11to 1.09±0.11 inferring excellent flow property.

Table 8 Precompression parameters of the powder blend of aceclofenac containing solid dispersions by kneading method

Formulation code	Angle of repose(Ø)	Bulk density gm/cm^3	Tapped density (gm/cm^3)	Hausner's ratio	Carr's index(%)	Assay (%)
SDKM1	36.0±0.11	0.426±0.09	0.375±0.11	0.88±0.11	13±0.12	97.26±0.11
SDKM2	39.0±0.10	0.426±0.10	0.364±0.10	1.02±0.15	17±0.11	98.41±0.10
SDKM3	36.0±0.15	0.478±0.11	0.395±0.09	1.04±0.10	21±0.10	96.69±0.12
SDKM4	37.0±0.12	0.456±0.06	0.374±0.08	1.02±0.16	21±0.09	98.89±0.10
SDKM5	38.0±0.08	0.342±0.08	0.310±0.06	1.0±0.08	10±0.10	97.55±0.09

The angle of repose of above formulations ranged between 34.0±0.11 to 40.0±0.14 inferring fair flow property. Carr's index ranged from 1±0.12 to 15±0.17 inferring good flow property. Hausner's ratio ranged from 1.10±0.10 to 1.20±0.09 inferring good flow property.

Table 9 Precompression parameters of the powder blend of aceclofenac containing solid dispersions by solvent evaporation method

Formulation code	Angle of repose(Ø)	Bulk density gm/cm^3	Tapped density (gm/cm^3)	Hausner's ratio	Carr's index(%)	Assay (%)
SDSEM1	36.0±0.10	0.396±0.10	0.355±0.08	1.11±0.11	11±0.11	97.24±0.14
SDSEM2	34.0±0.11	0.385±0.15	0.386±0.09	1.13±0.10	10±0.15	98.25±0.14
SDSEM3	37.0±0.14	0.401±0.11	0.425±0.10	1.10±0.08	5±0.09	97.66±0.10
SDSEM4	35.0±0.12	0.420±0.13	0.415±0.11	1.12±0.10	1±0.12	98.41±0.11
SDSEM5	40.0±0.13	0.410±0.11	0.418±0.09	1.18±0.14	1±0.14	97.42±0.13

The precompression parameters were found to be good as related to other formulations. The solubility of the drug is increased markedly and is nearer to that of the optimized formulation SDSEM5 (0.331±0.006 mg/ml). PEG 4000 is a hydrophilic nonionic surfactant; hence it enhances the solubility of the drugs having poor solubility, by imparting its hydrophilic nature.

4.3.4 CrystallinitybyXRD

Thecrystallinityoftheprepared soliddispersions ofaceclofenacisstudied byXRD.Thechangein degree of crystallinity was studied. The pure drug and solid dispersions were also analyzed by XRD in same manner and the peak intensity and presence of new peaks were noted. The XRD pictures are depicted in Figures 7 & 8for pure drug and SDSEM5 respectively.

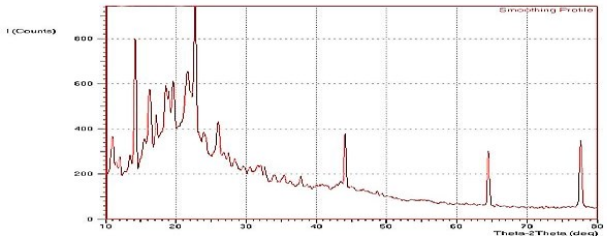

Figure 7: XRD of pure drug

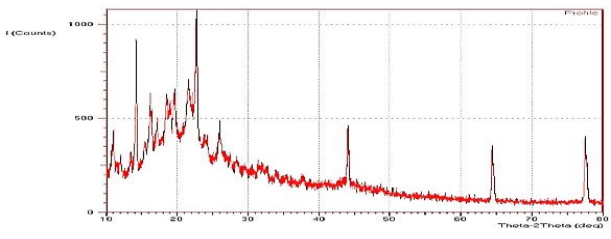

Figure 8: XRD of SDSEM5

4.3.5 In-vitrodissolutionstudiesin6.8pHphosphate buffer

From the above dissolution studies, formulation SDSEM5-aceclofenac by solvent evaporationmethod with PEG 4000 in 1:5 ratio showed 99% release in 30 minutes in 6.8 phosphate buffer when compared to pure drug which may be due to increased wettability of the drug by using such hydrophiliccarriersandmoredruggettingavailablefordissolution.Pureaceclofenacdueits hydrophobicnatureand poorsolubilitytendsto form aggregatesand float on thesurface leadingto reducedeffectivesurfaceareaandtherebydecreaseddissolution.Itwasalsoevidentthatasthe PEG 4000 concentration got increased, the release of aceclofenac from the SEM got increaseddue to more carriers available for coating. Hence, SDSEM5 was taken as optimized formulation.

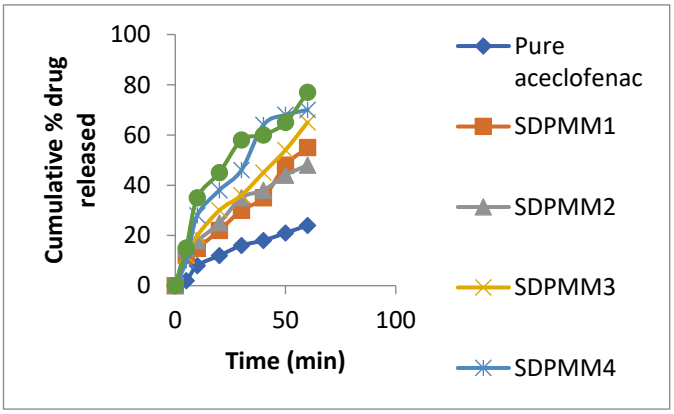

Figure 9:Dissolutionprofilesof aceclofenacSDsby Physical mixture method (PMM)with PEG 4000

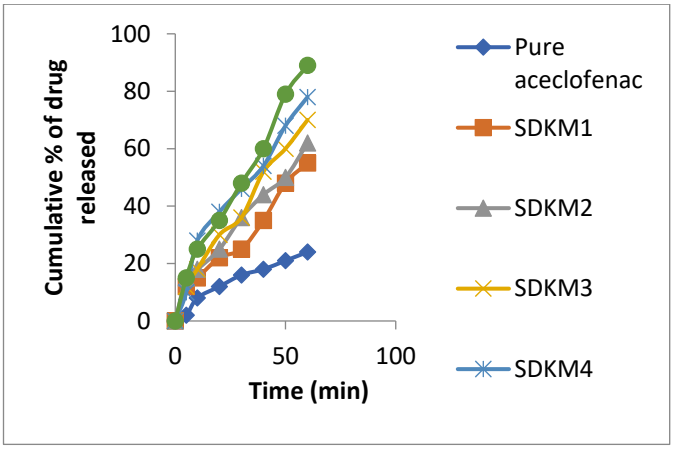

Figure 10: Dissolution profilesofaceclofenacSDsby kneading method (KM)with PEG 4000

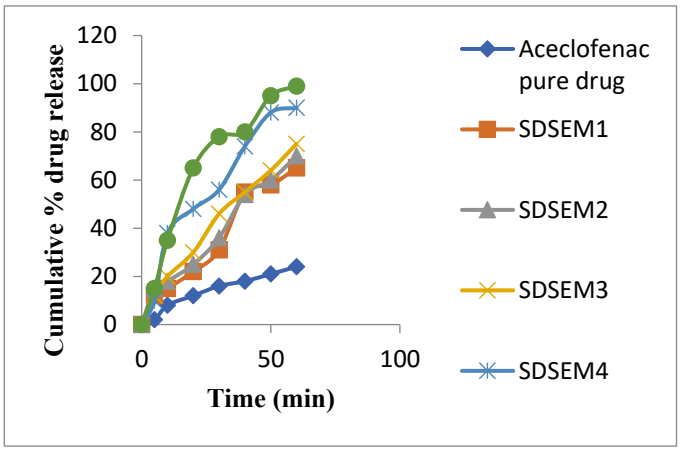

Figure11: Dissolution profilesofaceclofenacSDsby solvent evaporation method (SEM)with PEG 4000

4.4 Preparation of tablets using prepared aceclofenac solid dispersions

Tablet of the aceclofenac solid dispersion was prepared with the one that showed maximum drug release. The ingredients along with their quantities are depicted in table 10.

Table 10: Formulafor SDSEM5 Tablet

S. No.	Nameof the ingredient	Quantity(mg)
1.	Drug(equivalent amount of solid dispersion) (mg)	598
2.	Microcrystallinecellulose (2%)	13
3.	PVP(2%)	13
4.	Mg.stearate(2%)	13
5.	Talc (2%)	13
6.	**TotalWt. (mg)**	**650**

4.5 Evaluationofaceclofenactablets

4.5.1 Performance evaluation of tablet

The optimized solid dispersions in 1:5 ratio containing PEG 4000 (SDSEM5) was prepared by solvent evaporation method, showed better results compared to other formulations. Hence tablets of the formulation SDSEM5 were prepared by direct compression method. Tablets were evaluated for various parameters like weight variation, hardness, friability, drug content, disintegration time and in vitro drug release studies.

The hardness of the tablets was found to be to 5 ± 0.11 kg/cm^2 and friability was found to be below 1% indicating good resistance. All tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. 498 ± 5 %. The drug content was found to be 99.14 ± 13%, indicating uniform distribution of drug in the tablets. The most important parameter that needs to be optimized in the development of tablets is the disintegration time of tablets. In the present study, disintegration time of found to be 10 min. It was observed that less disintegration time was observed when PEG 4000 was used as carrier, may be due to swelling at faster rate upon contact with water. Dissolution studies were performed in 6.8 pH phosphate buffer. FormulationSDSEM5 showed maximum percentagedrugrelease99.62 ± 0.15% in 30 minutes in 6.8pHphosphate buffer asshown in Figure 12andresultsshown in Table11.

Table11:Evaluation of tablet containing SDSEM5

Tablet Parameters	FormulationSDSEM 5
Weight variation(mg)	498±5
Hardness(kg/cm^2)	5±0.11
Friability(%)	0.438±0.15
Disintegrationtime(min) *	10±0.15
Content uniformity (%)	99.14±13

*Percentagedrugreleased ±SD (n=4)

The stability of the optimized formulation SDSEM5 tablets was known by performing stability studies for one month at accelerated conditions of 40±0.69°C/75±2% RH on optimizedformulation. The formulation was found to be stable, with insignificant change in the hardness, disintegration time, drug content and in-vitro drug release in 6.8 pH phosphate buffers.

4.5.2 In-vitrodissolution studies of prepared aceclofenac tablets (SDSEM5) with marketedtablet (Xerodol® 100mg)

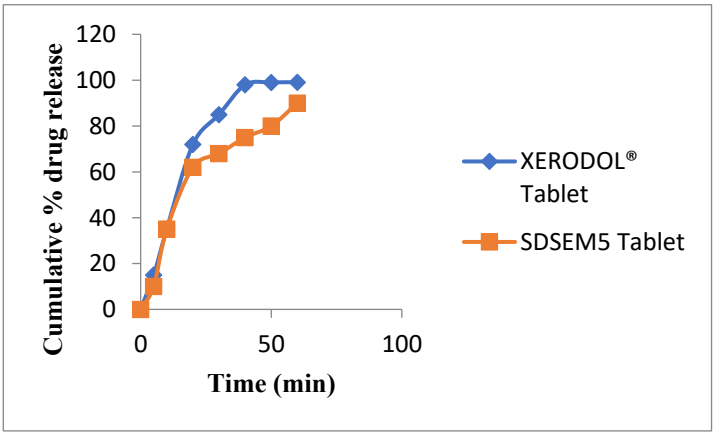

Figure12: Dissolutionprofiles of aceclofenacSDsby solvent evaporation method (SEM)with PEG 4000

5. DISCUSSION

Present research work encompasses development and evaluation of poorly soluble drug aceclofenac with PEG 4000 as carrier by physical mixture, kneading and solvent evaporation methods. The research objective was divided in to preformulation study, optimization development and preparation of solid dispersion using different methods formulation of solid dispersion in tablet dosage form and comparison with marketed Xerodol® formulation for its release.

Melting point of the drug aceclofenac was determined as 152.7 °C which was complied with reported value 149-153°C in the published article for its identification

The analytical method was validated on UV 1800, Shimazu and the method was found easy, accurate and precise from analysis point of view with Linear dynamic range 0.1-0.7 µg/mL, Regression equation y = 0.4714x - 0.0143, Correlation coefficient R^2 = 0.998, SE intercept 0.005, SD intercept 0.012, LOD (µg/mL) 0.24 LOQ (µg/mL) 1.05 and Variance of the calibration line 0.05. The λmax of aceclofenac was found as 271 nm in methanol.

Solubility of the pure drug aceclofenac was determined as 65.28±0.015 µg/mL in water indicating as poorly soluble drug. The solubility was complied with the reported solubility of aceclofenac 58 µg/mL.

Appearance of characteristic troughs in DSC thermograms cleary indicated that there was no interaction found between the drug aceclofenac and the carrier PEG 4000 indicating aceclofenac was compatible with PEG 4000.

Solid dispersions of drug aceclofenac were prepared with PEG 6000 in varying proportions from 1:1 to 1:5 using different methods (physical mixture, kneading and solvent evaporation).

Prepared solid dispersions were evaluated for assay, solubility, dissolution studies and pre-compression parameters. Based on the data obtained from the study SDSEM5 solid dispersion containing 1:5 of aceclofenac and PEG 4000 was found as the best optimized solid dispersion as it released the drug content higher than the others.

Solubility of the prepared solid dispersions were found to be increased with increased ratio of PEG 4000. The maximum solubility of aceclofenac was observed in SDSEM5 prepared by solvent evaporation method using drug and polymer ratio (1:5). The solubility of the drug is increased markedly and is nearer to that of the optimized formulation ACP415SM (0.331±0.006 mg/ml). Poloxamer407 is a hydrophilic nonionic surfactant; hence it enhances the solubility of the drugs having poor solubility, by imparting its hydrophilic nature.

The prepared solid dispersions complied with the requirements of assay. The result for assay for SDSEM was 99.14±13%. These percentage drug values indicated that the drug content is uniform in all the batches. Formulation SDSEM5 showed maximum assay value than other formulations.

The angle of repose of the solid dispersion formulations prepared by physical mixture method ranged between 34.0±0.12 to 42.0±0.11inferring fair flow property. Carr's index ranged from 10±0.10 to 21±0.10 inferring fair flow property.Hausner's ratio

ranged from 0.88±0.11to 1.09±0.11 inferring excellent flow property.

The angle of repose of the solid dispersion formulations prepared by kneading method ranged between 34.0±0.11 to 40.0±0.14 inferring fair flow property. Carr's index ranged from 1±0.12 to 15±0.17 inferring good flow property. Hausner's ratio ranged from 1.10±0.10 to 1.20±0.09 inferring good flow property.

The precompression parameters of the solid dispersion formulations prepared by solvent evaporation method were found to be good as related to other formulations.

Thecrystallinityofthepreparedsoliddispersions ofaceclofenacisstudied byXRD.Thechangein degree of crystallinity was studied. The pure drug and solid dispersions were also analyzed by XRD in same manner and the peak intensity and presence of new peaks were noted. The XRD pictures are depicted in Figures 5.8 & 5.9for pure drug and SDSEM5 respectively. The results indicated no presence of any crystalline form of the drug.

In vitro dissolution of the prepared solid dispersions was compared with each other and with that of the pure drug. Maximum drug release was observed with SDSEM5 % in comparison to pure drug for which the drug release observed were %.

Tablets were prepared with SDSEM5 solid dispersion as per the formula depicted in table in which microcrystalline cellulose (2%) was used as disintegrant, PVP (2%) as binder, Mg. stearate (2%) as lubricant and Talc (2%) as glidant. Tablets were evaluated for various parameters like weight variation, hardness, friability, drug content, disintegration time and in vitro drug release studies. The hardness of the tablets was found to be to 5 ± 0.11 kg/cm^2 and friability was found to be below 1% indicating good resistance. All tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. 498 ± 5 %. The drug content was found to be 99.14 ± 13%, indicating uniform distribution of drug in the tablets. The most important parameter that needs to be optimized in the development of tablets is the disintegration time of tablets. In the present study, disintegration time of found to be 10 min. It was observed that less disintegration time was observed when PEG 4000 was used as carrier, may be due to swelling at faster rate upon contact with water. Dissolution studies were performed in 6.8 pH phosphate buffer. FormulationSDSEM5 showed maximum percentagedrugrelease99.62 ± 0.15% in 30 minutes in 6.8pHphosphate buffer asshown in Figure 5.12andresultsshown in Table5.11.

Prepared tablet containing SDSEM5 solid dispersion were evaluated and compared with marketed Xerodol® formulation for the dissolution profile. Prepared tablets exhibited comparable extent of drug release with marketed Xerodol® tablet formulation.

6. CONCLUSIONS

Solid dispersions of the drug aceclofenac were prepared with carrier PEG 6000 using different methods physical mixture, kneading and solvent evaporation. Solid dispersions prepared with solvent evaporation method exhibited better drug solubility and drug content along with acceptable pre-compression parameters and dissolution profile. Drug polymer compatibility test indicated towards no

interaction between the same. Dissolution of the prepared tablets with selected solid dispersion exhibited comparable extent of drug release. Therefore, solid dispersion prepared with PEG 6000 in a ratio of 1:5 can be selected for better. The solid dispersion showed significant enhancement in aqueous solubility and in vitro drug release compared to the pure drug. Physicochemical characterization using FTIR, DSC, and XRD confirmed the absence of chemical interaction and a reduction in drug crystallinity, which contributed to the improved performance. The optimized formulation exhibited uniform drug content, good flow properties, and excellent stability under accelerated conditions. Thus, the preparation of aceclofenac solid dispersion offers a promising approach for enhancing its oral bioavailability, potentially leading to improved therapeutic efficacy and better patient compliance. In conclusion, solid dispersion is a valuable and reliable formulation approach for addressing the challenges of poor aqueous solubility and slow dissolution associated with aceclofenac, and it can be extended to other BCS Class II drugs as well.

7. FUTURE PROSPECTIVE

To improve solubility, stability, and controlled release, new polymeric carriers like Soluplus®, Kollidon VA64, or Eudragit variants can be added. Utilizing natural and biodegradable polymers could provide safer and more environmentally friendly substitutes. Solid dispersions that are nanosized can offer increased surface area, quick absorption, and even better bioavailability. For scaling up, methods like supercritical fluid processing and nanoprecipitation can be investigated. By using solid dispersion, controlled-release or targeted delivery systems can be developed to minimize side effects and decrease the frequency of doses. Possible incorporation for site-specific delivery into gastroretentive or mucoadhesive systems can be undertaken in future. For commercial viability, concentrate on scalable and reasonably priced production techniques such as spray drying and hot-melt extrusion. Stability and shelf-life optimization may be undertaken to satisfy legal and industrial requirements.

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