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FORMULATION AND EVALUATION OF ACECLOFENAC MATRIX TABLETS USING SOLID DISPERSED PRODUCT

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Keywords:

Aceclofenac, BCS class II, Solid dispersion, Matrix tablets, Wet Granulation.

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ABSTRACT: Aceclofenac is a non-steroidal anti-inflammatory drug indicated for symptomatic treatment of pain and inflammation. Aceclofenac is a BCS Class II drug with low solubility and high permeability, thus solid dispersion is one of the promising techniques used for enhancement of solubility and dissolution rate. The intent of the present study was to formulate and evaluate aceclofenac matrix tablets by Wet Granulation technique, by partial in-corporation of the solid dispersed product as loading dose and pure drug as maintenance dose; so that the initial loading dose will produce an immediate therapeutic effect and the pure drug will lead to maintaining the concentration within the therapeutic index. Solid dispersions of aceclofenac were prepared by solvent evaporation method by using two different carriers klucel Hydroxy Propyl Cellulose–EXF and Hydroxyl Propyl Methyl Cellulose K-100 M CR by varying the drug and polymer ratios. Aceclofenac matrix tablets were formulated by wet granulation technique and all the formulations were evaluated for pre-compression and post-compression parameters. The granules showed good flow properties. All the formulated tablets were found within the permissible limits for various Post-compression parameters. The drug content and drug release profile were maximum in the SD2 formulation of 1:1 ratio in both pH 1.2 0.1N HCl and 6.8 pH phosphate buffers. The in-vitro drug release of PH4 formulation showed the best release of 96.79 % at 24 hrs. Formulation of aceclofenac matrix tablets using solid dispersed products seems to be a promising formulation for the safe and effective delivery in the treatment of pain and inflammation.

INTRODUCTION: Among the many types of routes of administration, the oral route is the most preferred choice for the administration of varieties of medications due to its ease of administration, convenience, low cost and patient compatibility. This type of delivery system is an example for conventional drug delivery system and these conventional dosage forms have the ability to facilitate the immediate release of the drug, these immediate release formulations results in faster drug absorption, multiple drug therapy increases the chance of toxicity and leads to poor patient compliance. There are many strategies to overcome these types of drawbacks associated with conventional dosage forms. Among them, the concept of a novel drug delivery system proves to

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be an ideal way for the development of matrix tablets. Matrix tablets are a significant approach for the development of modified drug delivery systems. Matrix tablets can be defined as the "oral dosage forms in which the active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices [1].

Advantages of Matrix Systems:

- Reduction in dosing frequency results in prolonged drug release.
- Drug accumulation is minimized
- Improved Patient compliance
- Minimization of health care cost

Disadvantages of Matrix Systems:

- Requirement of inert ingredients for the preparation of matrix tablets
- Gastric transit time and the presence of food leads to an alteration in the drug release profile
- High production cost

Ideal Characteristics of Drug Acceptable For Matrix Tablet

- Molecular size should be less than 1000 Daltons
- Elimination half-life should be in the range of 2 to 8 hrs
- Oral bioavailability should be more than 75 %.
- Therapeutic index should be high [2].

Aceclofenac is a potent non-steroidal anti-inflammatory drug commonly prescribed for treating rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Chemically aceclofenac is represented as [2-(2, 6-dichlorophenyl) amino] phenylacetyl oxyacetic acid, possessing analgesic activity. It is the analogue of diclofenac and has low gastrointestinal side effects. It is a white crystalline solid and is insoluble in water but freely soluble in acetone and ethanol. It is well absorbed orally, and the oral bioavailability is almost 90-95 %. The half-life of aceclofenac is 4-6 h and approximately 70-80 % of the drug is excreted by the renal route. Aceclofenac belongs to BCS class II with low aqueous solubility and high permeability, which leads to poor drug dissolution and insufficient bioavailability. Therefore, the enhancement of solubility and dissolution rate seems to be a challenging factor. Thereby, various strategies like polymorphism, micronization, and solid dispersion techniques have been adopted to improve the solubility and dissolution rate of poorly soluble drugs [3]. Solid dispersion is one of the most feasible and fruitful techniques to increase the drug release profile of poorly soluble drugs. The theory of solid dispersion was first introduced by Sekiguchi and Obi in 1961. The term solid dispersion refers to "a group of solid products consisting of at least two different moieties, especially hydrophobic drug, and a hydrophilic matrix, where the matrix can be either amorphous or crystalline, and the drug can be homogeneously dispersed in crystalline or amorphous particles [4]. Thus solid dispersion technique is widely used to enhance the solubility and bioavailability of poorly soluble drugs. The present study aims to formulate and evaluate matrix tablets using a solid dispersion technique to enhance their solubility and dissolution rate by using various polymers.

MATERIALS AND METHODS:

Materials: Aceclofenac was purchased from Empree Medicaments Belgaum. HPMC K 100 M CR was obtained as a gift sample from Colorcon Asia Pvt. Ltd, Goa, and Klucel HPC-EXF were obtained as a gift sample from Apotex Research Pvt. Ltd, Bangalore. Polyvinyl pyrrolidone K-30 (PVP K- 30) was purchased from Balaji Chemicals Pvt. Ltd, Mumbai. Lactose and Magnesium Stearate was purchased from Himedia. Pvt. Ltd, Mumbai. Talc was purchased from Ozone International Pvt. Ltd.

Methods:

Drug Identification:

Determination of λ_{max} of Aceclofenac in Both 1.2 pH 0.1N Hcl and 6.8 pH Phosphate Buffer: Aceclofenac (100 mg) was dissolved in 50 ml methanol, and volume was made up to 100 ml in the volumetric flask using different buffer solutions 1.2 pH Hcl and 6.8 pH Phosphate buffer to obtain a concentration of 1000 µg/ml (SS-I). From the stock solution, 100 µg/ml solution of aceclofenac was

prepared by doing suitable dilutions with the buffer and scanned between 200-400 nm.

Development of Standard Calibration Curve of Aceclofenac in Both 1.2 pH 0.1N HCl and 6.8 pH Phosphate Buffer: Aceclofenac 100 mg was accurately weighed and dissolved in 50 ml methanol, and volume was made up to 100 ml in the volumetric flask using different buffer solutions 1.2 pH Hcl and 6.8 pH Phosphate buffer. Further dilutions were made from the working standard drug solution with different pH buffer solutions to obtain the concentration of 2, 4, 6, 8, and 10 µg/ml of aceclofenac, and the absorbance was measured against blank at 275 nm using UV- visible spectrophotometer.

Solubility Analysis: Saturation solubility was done to determine the amount of drug dissolved in a solvent. Accurately weighed 100 mg of aceclofenac was dissolved in a beaker containing two different buffer solutions 1.2 pH Hcl and 6.8 pH Phosphate buffer (25 ml). Both the beakers were placed in a metabolic shaker for 24 h. After 24 h, the samples were sonicated for half an hour, and the solutions were filtered using Whatman filter paper; the filtered solutions were analyzed using UV- visible spectrophotometer at 275 nm 5.

Formulation of Aceclofenac Solid dispersion: Aceclofenac solid dispersion was prepared by a solvent evaporation method. A specific amount of drug and carriers such as klucel HPC-EXF and HPMC K 100 M-CR were weighed according to the two different ratios (1:1 and 1:2) and dispersed in 10 ml of 95% ethanol to obtain a translucent solution. The solvent was evaporated by continuously stirring on a water bath at 750 °C. The obtained solid residue was dried in a desiccator, pulverized, and passed through mesh no ^{40}. The resultant solid dispersed powder mixtures were incorporated into matrix tablets.

Evaluation of Solid Dispersed product: The formulated solid dispersed products were evaluated for the estimation of drug content and drug release profile.

Drug Content: A weighed amount of solid dispersed product equivalent to 100 mg of drug was dissolved in volumetric flasks containing two different buffer solutions, *i.e.* 1.2 pH Hcl and 6.8 pH Phosphate buffer (100 ml); from the above stock solution, 10 ml was withdrawn and diluted to 100 ml in a volumetric flask to obtain the concentration of 100 µg/ml. Further, 1 ml solution was withdrawn and diluted to 10 ml in a volumetric flask to get the concentration of 10 µg/ml. The absorbance of the solutions was measured against blank at 275 nm using UV spectrophotometer.

***In-vitro* Dissolution Studies:** The In-vitro dissolution studies were carried out using USP dissolution apparatus type II. A calculated amount of pure drug and solid dispersed product equivalent to 100 mg of pure drug was weighed, and the dissolution test was performed in both 1.2 pH Hcl and 6.8 pH phosphate buffer for 2 h. The temperature was maintained at 37 ± 0.5 °C with continuous stirring at the rate of 50 rpm. A sample of 5 ml was withdrawn at specific time intervals from 900 ml 1.2 pH Hcl and 6.8 pH phosphate buffer; the same volume was replaced with the fresh dissolution media. The samples withdrawn were filtered through Whatman filter paper and measured using UV Spectrophotometer at 275 nm 6.

Preparation of Aceclofenac Matrix Tablets by incorporating Solid Dispersed product: Matrix tablets containing solid dispersion of aceclofenac equivalent to 170 mg of pure drug was prepared by wet granulation technique. All the ingredients except magnesium stearate and talc were thoroughly mixed using and passed through sieve no ^{60}. The powder blend was granulated using 20 % PVP-K 30 solution as a granulating agent to form dough mass which was passed through sieve no 40. The prepared granules were dried in a hot air oven at 400 °C. After drying, the granules were passed through sieve no 20 (sieve opening: 841 µm) and mixed with magnesium stearate and talc. The resultant powder blends were compressed using a Remik mini press-I machine equipped with round flat punches of size 12 mm with the theoretical cut weight of 350 mg 7. The composition of different formulations was shown in **Table 1.**

Evaluation of Powder Blend:

Angle of Repose: The funnel technique was used to determine the angle of repose of granules. The granules were allowed to freely flow out of the funnel onto the surface. The diameter of the

powder cone was measured, and angle of repose was calculated using the following equation

$$\text{Tan } \theta = h/r$$

Where 'h' is height of the pile and 'r' is the radius of the powder base

Bulk and Tapped Density:

Bulk Density: It was measured by pouring the weighed powder into a measuring cylinder, and the volume is noted. It is expressed in g/ml and is calculated by using this formula

Bulk Density (g/ml) = Mass of the Powder/ Bulk Volume

Tapped Density: Tapped density was measured by tapping the powder blend to constant volume by using a measuring cylinder. It is expressed in g/ml and is calculated by using this formula.

Tapped Density (g/ml) = Mass of the Powder/ Tapped Volume

Compressibility Index and Hausner's Ratio: The Compressibility Index of the powder blend was determined by Carr's Index. Based on the apparent bulk density and tapped density, the percentage compressibility of the blend was determined using the following formula.

% Compressibility = [(Tapped density – Bulk density) / Tapped density] ×100

Hausner's ratio indicates the ease of powder flow. It is calculated by the following equation

Hausner's ratio = tapped density/ bulk density [8]

Physical Evaluation of Aceclofenac Matrix Tablets: The following quality control tests were performed on all the developed matrix tablets.

Thickness and Diameter: The thickness and diameter of the tablets of all the formulations was measured by using Vernier caliper. It is expressed in mm.

Hardness: The hardness of the tablet signifies its strength and indicates the capability of a tablet to resist mechanical shocks during processing and handling.

The hardness of tablets of all the formulations was determined by using Monsanto hardness tester. It is expressed in kg/cm^{-2}.

Friability: Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used to determine the friability of the tablets. The samples of twenty tablets were pre-weighed accurately on a digital weighing balance. The weighed tablets are placed in the drum of Roche friabilator. The friabilator is allowed to rotate for 100 revolutions (the revolution speed of friabilation is 25 rpm). The tablets are dusted and removed from the drum. These tablets are dusted and weighed again. The difference between the initial weight of the tablets (W1) and the weight of the tablets after subjecting to friabilator (W2) gives the friability of the tablet. Compressed tablets should not lose more than 1% of their weight.

% Friability = (Initial weight - Final weight)/ Initial weight x 100

Weight Variation: The weight variation test is used to confirm that the weight of tablets in a batch is consistent. The total weight of randomly selected 20 tablets from each formulation is determined, and the mean is calculated. Similarly, the weight of the individual tablet is also determined to find out the weight variation [9].

Drug Content Analysis: A weighed amount of crushed powder equivalent to 200 mg of drug was dissolved in volumetric flasks containing two different buffer solutions *i.e*. 1.2 pH Hcl and 6.8 pH Phosphate buffer (100 ml); from the above stock solution, 10 ml was withdrawn and diluted to 100 ml in a volumetric flask to obtain the concentration of 100 µg/ml. Further, 1 ml solution was withdrawn and diluted to 10 ml in a volumetric flask to get the concentration of 10 µg/ml. The absorbance of the solutions was measured against blank at 275 nm using a UV spectrophotometer.

***In-vitro* Dissolution study:** The release of the drug from different batches of prepared tablets was studied by using USP dissolution apparatus type II (paddle type) in both 1.2 pH HCl and 6.8 pH Phosphate buffer. The dissolution medium used was 900 ml of 1.2 pH 0.1N HCl for 2 hours and 6.8 pH Phosphate Buffer for 3-24 h. The temperature was maintained at 37 ± 0.50 °C with continuous stirring at the rate of 50 rpm. 5 ml of the samples were withdrawn from the media at the pre-determined intervals, and the same volume was

replaced with the fresh dissolution medium. The samples withdrawn were filtered through Whatman filter paper and were measured by UV Spectrophotometer at 275 nm [10].

Short Term Stability Studies: Stability of a drug is defined as the ability of a particular formulation in a specific container to remain within its physical, chemical, therapeutic and toxicological specifications.

The purpose of stability studies is to determine how the quality of formulation varies with time under various environmental factors such as temperature, humidity, and light.

A short-term stability study was performed at both room temperature and accelerated temperatures. The tablets were stored in amber-colored bottles and tightly plugged with cotton and capped. The room temperature storage condition was 25 ± 2 °C and 65% RH and in case of accelerated stability studies, the tablets in bottles were placed in a humidity chamber at a temperature of 40 ± 2 °C at Relative Humidity of 75 ± 5%. At regular time intervals of 30 days, tablets were analyzed for hardness, friability, drug content, and in-vitro drug release [11].

RESULTS AND DISCUSSION:

Spectral Analysis: The absorption spectrum of the pure drug was scanned over the range of 200 – 400 nm with (100 mcg/ml) concentration prepared in 1.2 pH 0.1 N HCl and pH 6.8 phosphate buffer. The absorption spectra of aceclofenac showed only one peak at 275 nm in 1.2 pH 0.1 N HCl and 274.5 nm in pH 6.8 phosphate buffer, which represents the maximum absorption (λmax) of the drug.

Standard Calibration Curve of Aceclofenac: The Standard calibration curve of aceclofenac was carried out by a UV absorption spectrophotometer. The required solutions were prepared in buffer solutions at two different pH ranges: 1.2 pH 0.1N HCl and 6.8 pH phosphate buffer. The calibration curve obtained for aceclofenac showed good linearity with a regression coefficient (R2) value of 0.997 in 1.2 pH 0.1N HCl and 0.993 in 6.8 pH phosphate buffer over the concentration range of 2–10 µg/ml passing through the origin. The standard curve of aceclofenac is depicted in **Fig. 1.**

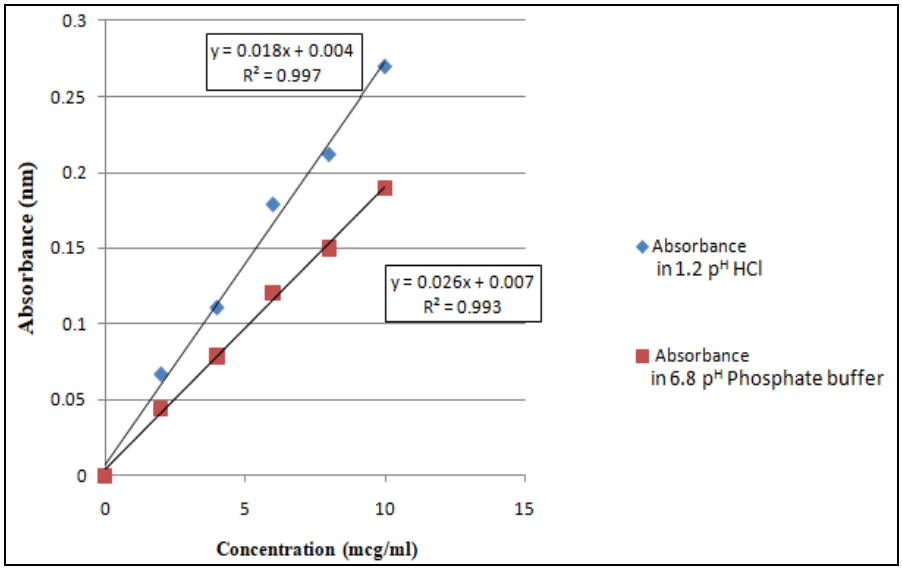

FIG. 1: STANDARD CALIBRATION CURVE OF ACECLOFENAC

Solubility Studies of Aceclofenac: The solubility studies of aceclofenac were carried out individually in two different buffer solvents at different pH ranges, 1.2 pH 0.1N HCl and 6.8 pH Phosphate buffer. The solubility of aceclofenac in 1.2 pH 0.1N HCl was found to be 0.228 mg/ml, whereas in 6.8 pH phosphate buffer, the solubility was found to be 2.868 mg/ml. From the results of solubility studies, it can be concluded that there was a slight decrease in solubility at 1.2 pH; since the pH was elevated to 6.8 pH, there was an increase in solubility. Hence, pH-dependent solubility is probably attributed to the acidic nature of the drug being an acetic acid derivative.

Formulation Batches of Aceclofenac Solid Dispersed Product: Four different batches of aceclofenac solid dispersed product were prepared by using two different carriers HPMC K 100 M-CR and klucel HPC-EXF, by varying the ratios as 1:1 and 1:2 shown in **Table 1.**

TABLE 1: FORMULATION BATCHES OF ACECLOFENAC SOLID DISPERSED PRODUCT

Formulation Code	Drug: Polymer Ratio	Aceclofenac (gms)	HPMC K-100 MCR (gms)	Klucel HPC-EXF (gms)
SD1	1:1	1gm	-------	1gm
SD2	1:1	1gm	1gm	-------
SD3	1:2	1gm	--------	2 gm
SD4	1:2	1gm	2gm	--------

Evaluation of Aceclofenac Solid Dispersed Product:

Drug Content Analysis: The weighed quantity of solid dispersed products were subjected for drug content analysis, and from the results of drug content analysis, it was found to be within the acceptable limits, as the limit is 90-110 %. Higher drug content was found in SD2 formulation, indicating a homogenous dispersion of drug within the carrier. The results of drug content analysis of solid dispersed products are presented in **Table 2.**

TABLE 2: DRUG CONTENT ANALYSIS OF ACECLOFENAC SOLID DISPERSED PRODUCT

Ratios	Formulation Code	Drug Content in 0.1N HCL (%)	Drug Content in 6.8 pH Phosphate Buffer (%)
	SD1	93.6	95.5
1:1	SD2	97.89	99.4
1:2	SD3	94.31	96.2
	SD4	97.5	98.8

***In-vitro* Dissolution Studies:** The drug release profile of aceclofenac solid dispersed product revealed better than the pure drug. The maximum release rate was observed in SD1, and SD2 formulations containing a minimum concentration of polymers, and ultimately the solid dispersed product formed was found to be less viscous and less elasticized, and hence the particle size was finely reduced, due to which these formulations showed best release profile. Whereas in SD3 and SD4 formulation, the percentage drug release was less as compared to SD1 and SD2 formulation. These formulations, *i.e.*, SD3 and SD4 contain the maximum concentration of polymers, which leads to the formation of highly viscous and more elasticized solid dispersed product and due to this reason, the particle size was not finely reduced, and thus SD3 and SD4 formulations showed less release profile when compared to SD1 and SD2. Among all the solid dispersed formulations, SD1 and SD2 were selected as ideal a formulation incorporated in the formulation of Matrix tablets. A comparative data of drug release profile in two different buffers were illustrated in **Fig. 2a** and **2b.**

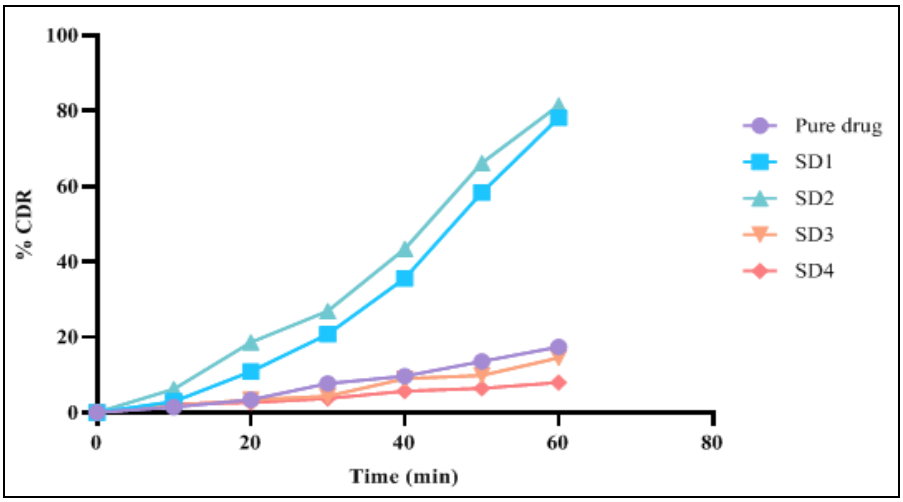

FIG. 2A: DRUG RELEASE PROFILE OF ACECLOFENAC SOLID DISPERSED PRODUCT IN 1.2PH 0.1N HCL

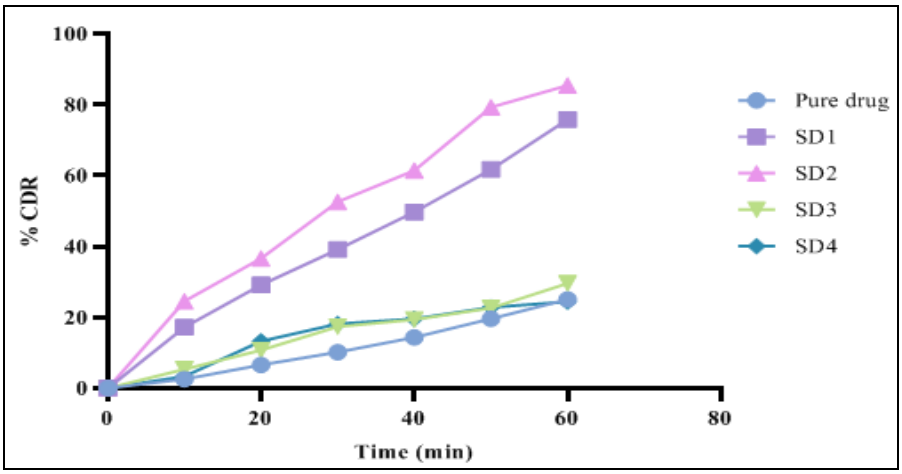

FIG. 2B: DRUG RELEASE PROFILE OF ACECLOFENAC SOLID DISPERSED PRODUCT IN 6.8 PH PHOSPHATE BUFFER

Preparation of Aceclofenac Matrix Tablets: Four different formulations of aceclofenac matrix tablets were prepared by wet granulation technique by incorporating selected solid dispersed formulation. The composition of different formulations was shown in **Table 3.**

TABLE 3: FORMULATION TABLE OF ACECLOFENAC MATRIX TABLETS USING SOLID DISPERSED PRODUCT

Ingredients	Formulation Code			
	PF1	PF2	PF3	PF4
Aceclofenac IP	200 mg	200 mg	170 mg	170 mg
Solid dispersed product of HPMC K-100 M CR	-	-	-	60 mg
Solid dispersed product of klucel HPC-EXF	-	-	60 mg	-
Plain HPMC K-100 MCR	-	100 mg	-	-
Plain klucel HPC-EXF	120 mg	-	-	-
Lactose	27 mg	47 mg	117 mg	117 mg
Magnesium Stearate	2 mg	2 mg	2 mg	2 mg
Talc	1 mg	1 mg	1 mg	1 mg
Cut Weight (mg)	350 mg	350 mg	350 mg	350 mg

Studies on Pre – Compression Blend: The flow properties of the powder blend such as angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio, were carried out for matrix formulations (PF1 – PF4). The data obtained it states that the angle of repose was found to be in the range of 250 - 300, indicating the excellent flow property. The bulk density of all the four formulations was found to in the range of 0.465 - 0.606 gm/cm^{-3}, while the results of tapped density were found to be in the range of 0.518 - 0.673 gm/cm^{-3}. Carr's index of all the formulations ranged between 8.71 % - 11.74%, and Hausner's ratio was found to be in the range of 1.10-1.13. All these values signify that the prepared powder blend presented a good flow property. The results of the pre-compression blend are represented in **Table 4.**

TABLE 4: PRE - COMPRESSION PARAMETERS OF ACECLOFENAC MATRIX TABLETS

Formulation Batch code	Bulk Density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Hausner's Ratio	Angle of Repose (θ)
PF1	0.465 ± 0.05	0.518 ± 0.03	10.23 ±0.49	1.11 ± 0.01	28.13 ± 0.43
PF2	0.545 ± 0.04	0.597 ± 0.05	8.71±0.67	1.10 ± 0.02	28.33 ± 0.95
PF3	0.606 ± 0.05	0.665 ± 0.04	8.87±0.34	1.10 ± 0.03	29.18 ± 0.64
PF4	0.594 ± 0.03	0.673 ± 0.05	11.74±0.29	1.13 ± 0.02	27.97 ± 0.53

Data is expressed in average of triplicate (n=3 ± SD)

Post – Compression Evaluation of Aceclofenac Matrix Tablets: The thickness and diameter of the tablet was found to be relatively consistent in all the formulation batches. The hardness of the tablets

for all the batch formulations ranged between 4.20 ± 0.12 to 4.51 ± 0.17 kg/cm^{-2} indicating good mechanical strength of the tablet. Results of the friability test for all the formulations were found to be within the acceptable range (less than 1%), which signifies the capability of a tablet to resist mechanical shocks and frictions. The average percentage deviation of all the formulations was found to be within the limits of ±5% of the weight. Hence, all the formulations complied with the test for uniformity of weight as per official specifications. The post-compression evaluation of aceclofenac matrix tablets for all the formulations is summarized in **Table 5.** The readings were obtained in triplicate, and values were presented as mean with standard deviation.

TABLE 5: POST - COMPRESSION PARAMETERS OF ACECLOFENAC MATRIX TABLETS

Formulation batch code	Diameter (mm)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)
PF1	12.02 ±0.01	3.27 ± 0.01	4.20 ± 0.12	0.57 ± 0.03	350.1 ± 0.31
PF2	12.08±0.02	3.05 ± 0.03	4.29 ± 0.17	0.68 ± 0.01	349.5 ± 0.25
PF3	12.12±0.05	3.12 ± 0.05	4.32 ± 0.15	0.77 ± 0.05	352.4 ± 0.18
PF4	12.05±0.07	3.52 ± 0.02	4.51 ± 0.17	0.87 ± 0.04	351.3 ± 0.25

Data is expressed in average of triplicate (n=3 ± SD)

Drug Content: Formulated aceclofenac matrix tablets were subjected for drug content analysis and the results of drug content analysis of all the formulations were found to be within the acceptable limits 90-110 %, indicating a homogenous dispersion of drug molecule within the polymer matrix in both 1.2 pH 0.1N HCl and 6.8 pH Phosphate buffer. The results of the drug content analysis of matrix tablets are presented in **Table 6.**

TABLE 6: DRUG CONTENT ANALYSIS OF ACECLOFENAC MATRIX TABLETS

Formulation batch code	Drug Content in 1.2pH 0.1N HCL Buffer	Drug Content in 6.8 pH Phosphate Buffer
PF1	94.16 ± 0.96%	93.10 ± 0.84%
PF2	95.54 ± 0.75%	95.47 ± 0.75%
PF3	96.29± 0.95%	94.26 ± 0.92%
PF4	97.53 ± 1.12%	96.60 ± 0.52%.

Data is expressed in average of triplicate (n=3 ± SD)

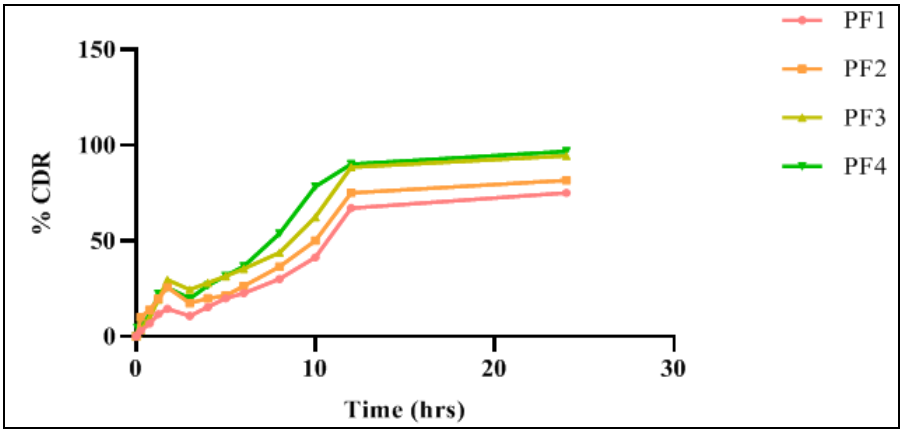

FIG. 3: *IN-VITRO* DRUG RELEASE PROFILE OF ACECLOFENAC MATRIX TABLETS

***In-vitro* Dissolution Studies:** Formulations containing aceclofenac as pure drug along with polymers such as klucel HPC-EXF and HPMC K-100 MCR (PF1 and PF2) showed a slight decrease in drug release profile at 24 h due to increased viscosity of the polymers, whereas the formulations containing pure drug incorporated into the solid dispersed product (PF3 and PF4) revealed increased drug release profile. *The in-vitro* drug release profile of PF3 and PF4 formulations was found to be maximum as compared to the other two formulations PF1 and PF2, due to intercalation of drug particles within the solid dispersed product which resulted in reduced particle size and thereby enhanced the dissolution rate of PF3 and PF4 formulations at 24 h.

Compared to the PF3 and PF4 formulations results, PF3 formulation showed decreased drug release rate due to slight intercalation within the solid dispersed matrix, which resulted in a slight reduction in particle size and hence there was a decrease in drug release profile. Drug release profiles of all these formulations are illustrated in **Fig. 3.**

Comparison of Dissolution Profile of PF4 with Marketed Formulation: The *in-vitro* drug release profile of PF4 formulation was compared with Marketed formulation AURFLUR- CR 200 mg, manufactured by FDC Limited. The PF4 formulation was selected as an ideal formulation for the comparative studies with the marketed formulation, as it has exhibited the maximum drug release rate as compared to other formulations. The *in-vitro* drug release profile of PF4 at 24 h was found to be 96.79 %, whereas the marketed formulation showed the release of 97.75 % at 24 h, indicating that PF4 formulation showed a similar release to the marketed formulation. The similarity factor (f2) was found to be 91. The drug release profile of PF4 and the marketed formulation was depicted in **Fig. 4.**

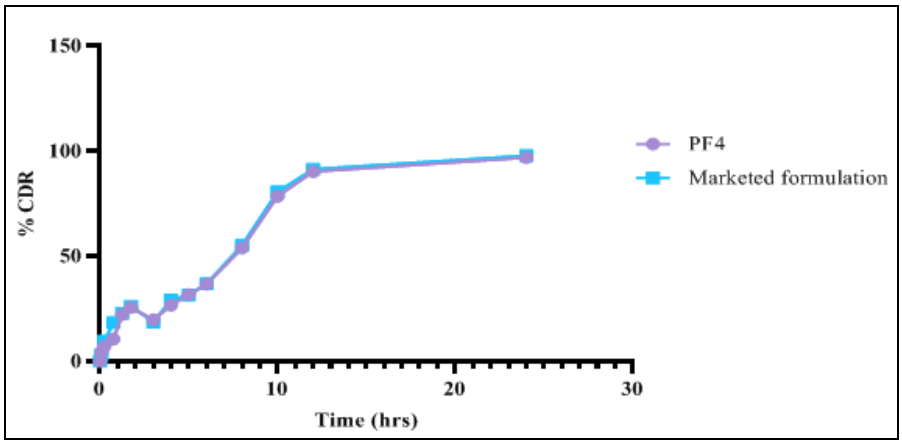

FIG 4: *IN-VITRO* DRUG RELEASE PROFILE OF PF4 FORMULATION AND MARKETED FORMULATION

TABLE 7: STABILITY PROFILE OF PF4 FORMULATION

Parameters	PF4 Formulation				
	Initial	Room Temperature 25 °C ± 2 °C / RH 60 ± 5%		Accelerated Temperature 40 °C ± 2 °C / RH 75 ± 5%	
		15 Days	30 Days	15 Days	30 Days
Hardness (kg/cm^2)	4.5	4.2	3.95	4.0	3.5
% Drug Content in 0.1N HCL	97.53 %	96.15%	95.10%	94.32%	93.89%
% Drug Content in 6.8 PB	96.60%	95.51%	94.95%	94.24%	92.68%
% CDR at 24 Hours	96.79%	95.12%	94.75%	94.15%	95.27%

Stability Studies: Stability studies were performed for matrix formulations as per ICH guidelines at room temperature (25 ± 20 °C and 65 ± 5% RH) and at accelerated temperature (40 ± 20 °C and 75 ± 5% RH) for a 30 days. The tablets were analyzed for Hardness, Drug content, and % Drug Release at the end of 15 days and 30 days. The formulations showed slight variations in hardness, drug content, and % drug release in accelerated conditions (40 ± 20 °C and 75 ± 5% RH). As the number of days increased, tablet hardness decreased due to reduced cohesion forces between particles, and loss of moisture from the tablet was also a reason to lose its hardness. The drug content of tablets in accelerated temperature was reduced due to slight degradation of the drug. The in-vitro release profiles of PF4 formulation at the end of 30 days were almost comparable, and there was no much difference observed. Thus the developed formulation was found to be stable at given storage conditions. The results of stability studies are tabulated in **Table 7.**

CONCLUSION: The absorption spectra of aceclofenac exhibited only one sharp peak at 275 nm in 1.2 pH 0.1 N HCl and 274.5 nm in pH 6.8 phosphate buffer, which represents the maximum absorption (λ_{max}) of the drug. The standard calibration curve obtained for aceclofenac showed good linearity with a regression coefficient (r^2)

value of 0.997 in 1.2 pH 0.1N HCl and 0.993 in 6.8 pH phosphate buffer over the concentration range of 2–10 µg/ml. The results of solubility studies highlighted a slight decrease in solubility at 1.2 pH, but as the pH was elevated to 6.8, there was an increase in solubility. Solid dispersions were prepared by using two different polymers klucel HPC EXF and HPMC K 100 M CR, by solvent evaporation method in two different ratios. Prepared solid dispersed products were analyzed for drug content uniformity and drug release profile. On the grounds of dissolution studies, two formulations were chosen for the preparation of aceclofenac matrix tablets. Matrix tablets were formulated by wet granulation technique and tablets were evaluated for pre-compression and post-compression studies.

The results of pre-compression studies revealed that powder mixtures are free-flowing and are suitable for compression. The results of post-compression studies signify that all the parameters are compliant with standard limits, and none of the parameters is significantly influenced by the variables. *In-vitro* dissolution studies showed that PF4 formulation exhibited maximum drug release compared to other formulations. Comparison dissolution studies were performed for PF4 formulation and marketed formulation; based on *in-vitro* drug release studies PF4 formulation showed similar release to the marketed formulation. Stability studies were performed for matrix formulations at room temperature (25 ± 20 °C and 65 ± 5% RH) and at accelerated temperature (40 ± 20 °C and 75 ± 5% RH) for 30 days. The data obtained from the stability studies indicate the developed formulation was found to be stable at given storage conditions. Thus, the formulated aceclofenac solid dispersed matrix tablets seem to be a promising formulation for the safe and effective delivery through the oral route in the treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis.

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