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DEVELOPMENT AND EVALUATION OF ACECLOFENAC SUSTAINED RELEASE MATRIX TABLETS

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ABSTRACT

The present investigation is concerned with development and evalution of Sustained release matrix tablets containing Aceclofenac using the hydrophilic polymer hydroxy propyl methyl cellulose (HPMC) & egg shell powder. Preformulation study was done initially which include characterization of polymers, drug identification, FTIR compatibility and result directed for the further course of formulation. The tablets were prepared by direct compression method and evaluation done. Tablets were compressed by tablet compression machine (Karnavati Rimek Mini press1) and evaluated with different parameters like diameter, thickness, average weight, hardness, friability, drug content, kinetic release data. The in-vitro release studies indicated that the sustained release matrix tablet dosage forms containing higher concentration of HPMC & Egg shell powder showed slower release. Concentration of alone HPMC & Egg shell powder when used significant less % cumulative release are occurs but when used in combination follow better release as required. The in-vitro release data was treated with mathematical equations, and it was concluded that aceclofenac released from the tablet followed zero order model. Hence sustained release drug delivery system of aceclofenac is a promising approach as it can lead to decrease in the frequency of administration and ultimately lead to better patient compliance.

KEYWORDS: Sustained release drug delivery system, aceclofenac, in-vitro drug release. Direct compression method.

INTRODUCTION[1,2,3,4,5,6,7,8,9,10]

Matrix tablets may be defined as the "oral solid dosage forms in which the drug or active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices which serves as release rate retardants". Oral controlled drug delivery systems represent the most popular form of controlled drug delivery systems for the obvious advantages of oral route of drug administration. Such systems release the drug with constant or variable release rates. Oral drug delivery system is the most widely utilized route of administration when compared to all other routes. Sustained release drug delivery provides most desirable dosing regimen. Sustained release indicates an initial release of drug sufficient to provide a therapeutic dose soon after administration, and then a gradual release over an extended period. Sustained release drug delivery system (SRDDS) have emerged as an effective means of enhancing the bioavailability and controlled delivery of many drugs. SRDDS play an important role in reducing the dosing frequency as well as by enhancing the biological half life of specific certain drugs. If the system is successful in maintaining constant drug levels in the blood or target tissue, it is considered as a controlled-release system. If it is unsuccessful at this but nevertheless extends the duration of action over that achieved by conventional delivery, it is considered as a prolonged release system. The oral route of administration for sustained release systems has received greater attention because of more flexibility in dosage form design. Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. The classification of matrix systems is based on matrix structure, release kinetics, controlled release properties (diffusion, erosion, swelling), and the chemical nature and properties of employed materials. Matrix system is widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. In fact, matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. During the last two decades there has been remarkable increase in interest in sustained release drug delivery system. The materials most widely used in preparing matrix systems include both hydrophilic and hydrophobic polymers. Commonly available hydrophilic polymers include Hydroxy propyl methyl lcellulose (HPMC), Hydroxy propyl cellulose (HPC), Hydroxy ethyl cellulose (HEC), Xanthan gum, Sodium alginate, Polyethylene oxide and cross-linked homo polymers and copolymers of Acrylic acid.

EXPERIMENTAL[11,12,13, 14,15,16,17]

Drug Authentication

General Description

The sample of Aceclofenac was evaluated for its physical state, odour and color.

Preformulation Studies of Aceclofenac

It is extensive information to bring out good quality at high standard at which optimal dosage desired. Preformulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

UV Spectroscopy

Preparation of Phosphate buffer pH 6.8

Weigh accurately 28.80gm of disodium hydrogen phosphate and 11.45gm of potassium dihydrogen phosphate dissolve in sufficient distilled water and make up the volume up to 1000ml with distilled water & filter.

Standard Curve of Aceclofenac

Aceclofenac has been quantitatively analyzed by various techniques. In present studies, Aceclofenac was estimated by UV Spectrophotometry method.

Preparation of Stock Solution

A solution of 1µg/ml Aceclofenac prepared by dissolving 100mg of a drug in 5ml of methanol and make up to 100ml with phosphate buffer pH 6.8 in a volumetric flask. Then the solution was diluted and the λmax of solution found in the range from 200-400nm. The absorbtion maximum was found to be 275nm.

Construction of Calibration curve of Aceclofenac in phosphate buffer

Weigh accurately 1mg of Aceclofenac and dissolve in 5ml of methanol and made upto 100ml with phosphate buffer pH 6.8 in a standared flask to get 10ug/ml solution. Then the solution was serially diluted to get 5, 10, 15, 20, 25µg/ml stock solution and the λmax of the stock was foun out. The absorbance of the solution was measured in a UV spectrophotometer at 275nm. A calibration curve was plotted by taking concentration of the solution in ug on X-axis and absorbance on Y-axis and co-efficient "r" was calculated.

Drug-Excipients Compatibility Studies

Drug-Excipients compatibility studies form an important part of Preformulation studies. The interaction between the drug and excipients are determined after a specific time period by using suitable analytical techniques like IR.

Infrared Absorption Spectroscopy

To investigate any possible interaction between the drug and polymer used (HPMC & Egg shell powder). Infrared spectra recorded on infrared spectrophotometer in KBr press IR spectrum of pure drug (Aceclofenac) and its physical mixture was carried out by using FT-IR.

FORMULATION DEVELOPMENT

a) Prepation of Egg shell polymer[13]

1) Egg shell particles preparation

The eggshell membrane was removed and the eggshell was washed thoroughly with tap water. Then the eggshell was boiled in deionized water for 30 minutes. It was dried in hot air oven at 80˚C for 2 h. The dried eggshell was crushed and ground using porcelain mortar and pestle. The eggshell powder which passed 200 mesh sieves was used in the study.

2) Treated egg shell particles preparation

20 g of the eggshell particles was treated with 20 mL of 1.0% w/v stearic acid solution in three different solvents, i.e., water, 95% ethanol or chloroform in glass mortar. In case of water, boiling water was used and the sample was dried in an oven at 45˚C overnight. In cases of ethanol and chloroform, the experiments were carried out at room temperature and the samples were left overnight at room temperature.

b) Preparation of Aceclofenac sustained release matrix Tablet

Matrix tablets containing Aceclofenac were prepared by direct compression technique using HPMC & Egg shell powder. Polymers and Aceclofenac were mixed homogeneously using glass mortar and pestle. Mixture were compressed into tablet by tablet compression machine (Karnavati Mini press-I) by using 12 mm punch to obtain tablets of desired specifications.

Table No.1: Composition of Aceclofenac sustained release matrix tablets.

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aceclofenac	200	200	200	200	200	200	200	200	200
Egg shell powder	-	-	-	160	140	130	100	80	60
HPMC	160	140	130	-	-	-	40	60	80
Lactose	140	160	170	140	160	170	160	160	160
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Povidone	190	190	190	190	190	190	190	190	190
Total weight	700	700	700	700	700	700	700	700	700

Evaluation Parameters[15,16,17]

Pre-compression evaluation parameters

- Angle of repose
- Bulk and tapped density
- Compressibility index and Hausner ratio.

Post-compression evaluation parameters

(Evaluation of compressed tablets)

- Thickness and appearance
- Hardness
- Friability
- Weight variation
- Uniformity of drug content
- In-vitro dissolution studies

Pre-compression evaluation parameters[15,16,17]

Bulk density and Tap density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Powder from each formulation, previously lightly shaken to break any agglomerates formed was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in volume was noted.

Bulk density is calculated by using a formula:

Bulk Density (g/ml) = weight of sample in gm / volume occupied by sample in ml.

The final volume was recorded and the tap density was calculated by the following equation:

$$\text{Tapped Density} = \frac{\text{Weight of powder blend}}{\text{Tapped Volume of the packing}}$$

Compressibility Index and Hausner Ratio

The Compressibility Index of the powder blend was determined by Carrs compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down.

$$\text{Compressibility Index} = \text{Bulk Density-Tapped Density} \div \text{Tapped Density} \times 100$$

$$\text{Hausner Ratio} = \text{Tapped Density} \div \text{Bulk Density}$$

Table No.2: Relationships between % Compressibility and Flow ability.

%Compressibility	Flowability	Hausner Ratio
5 – 15	Excellent	1.00 – 1.11
12 – 16	Good	1.12 – 1.18
18 – 21	Fair to Passable	1.19 – 1.25
23 – 35	Poor	1.26 – 1.34
33 – 38	Very Poor	1.35 – 1.45
> 40	Very Poor	1.46 – 1.59

Angle of repose[15,16]

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles, these frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle between the surface of a pile of the powder and the horizontal plane.

Angle of repose for blend of each formulation was determined by fixed funnel method. The funnel is secured with its tip with height h (2 cm), above a plane of paper kept on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the conical pile so formed just reaches the tip of funnel. Angle of repose was determined by substituting the values of the base radius and height of the pile 'h' in the given equation given below.

Where,

$\tan \theta = h/r$

θ = Angle of repose,

h = Height of pile,

r = Radius of base.

Table no.3: Relationships between Angle of repose and Flow property.

Sr. No.	Angle of repose	Flow property
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very poor

Pre-compression evaluation parameters

All the prepared matrix tablets were evaluated for following official and unofficial parameters.

Appearance

The tablets were identified visually by checking the difference in colour.

Thickness

Thickness of tablets was important for uniformity of tablet size. Thickness was measured by using vernier caliper on 3 randomly selected samples.

Hardness

Hardness of the all tablet formulations was determined by Monsanto hardness tester and precision dial type hardness tester. For each formulation the hardness of 5 tablets was determined, the average was calculated and presented with standard deviation. It is expressed in kg/cm^2.

Friability

Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the plastics chamber that revolves at 25 rpm for 4 mins dropping the tablets through a distance of six inches with each revolution. After 100 revolutions the tablets were reweighed and the percentage loss in tablet weight was determined:

$$\text{Percentage Friability} = \frac{W - W0}{W} \text{ X } 100$$

Where,

W0= initially weight

W= weight after friability

Percentages Friability of tablets less than 1% are considered acceptable

Weight variation test

Twenty tablets were randomly selected from each formulation and weighed individually to check for weight variation. The following percentage deviation in weight variation according to USP was allowed.

Table no. 4: Weight variation tolerances for uncoated tablets.

Sr. No.	Average mass	Percentage deviation
1.	130mg or less	±10
2.	More than 130 mg and less than 324 mg	±7.5
3.	324 mg or more	±5

In-vitro dissolution studies

Dissolution test was carried out using USP apparatus Type I Basket (electro lab) India. The dissolution medium consisted of 900 ml of phosphate buffer pH 6.8. Dissolution was performed at 37±0.5°C, with stirring speed of 100 rpm. 5ml of solution was withdrawn at time intervals of 5min, 15min, 30min, 1, 2, 3, 4, 5, 6, 7, 8 hrs filtered and replaced with 5ml of fresh dissolution medium each time. The collected samples were suitably diluted with dissolution fluid, wherever necessary and were analyzed for the aceclofenac at 275 nm by using a double beam UV spectrophotometer.

Release Kinetics of drug

All the formulations were subjected to study the release kinetics. The drug release profile of all the batches were fitted to

- Zero order kinetics
- First order kinetics
- Higuchi model
- Korsmeyer-Peppas model

To ascertain the kinetic modeling of drug release and the model with the higher correlation coefficient was considered to be the best fit model.

Zero Order Kinetics

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that area does not change and no equilibrium conditions are obtained) can be represented by the following equation,

$$f_t = Kt$$

Where, *f*t = the fraction of drug dissolved in time's

K = Rate Constant

t = Time

This model represents an ideal release profile in order to achieve the prolonged pharmacological action. This is applicable to dosage forms like transdermal systems, as well as matrix tablets with low soluble drugs, coated forms and osmotic systems.

First Order Kinetic

This model has also been used to describe absorption and/or elimination of some drugs, although it is difficult to conceptualize this mechanism in theoretical basis.

$$\mathbf{Log\ Q_t = log\ Q_0 + Kt/2.303}$$

Where Q_t = Amount of drug released in time't'.

Q_0 = Initial amount of drug in the solution.

K = Rate Constant.

Higuchi Model

This model is applicable to study the release of water soluble and low soluble drugs incorporated in semi-solid and/or solid matrices.

$$\boldsymbol{ft = Kt^{1/2}}$$

Where, *f*t = Amount of drug released in time't'

Koresmayer Peppas Model

This model is relating exponentially the drug release to the elapsed time (t):

$$\boldsymbol{ft = at^n}$$

Where, a = constant incorporating structural and geometric characteristics of the drug dosage form.

n = Release exponent

This model is widely used; when the release mechanism is not well known or when more than one type of release phenomenon could.

RESULTS

Preformulation study of Aceclofenac

Description

Colour - white to off-white

State - crystalline

Odour -plesant

Melting point

Melting point of Aceclofenac was found to be 149^0c

Solublity: It is insoluble water, freely soluble in acetone, soluble in methanol and ethanol.

UV Scanning

In Figure 6.1 observed that the drug was shown maximum maxima at 275nm in phosphate buffer pH 6.8.

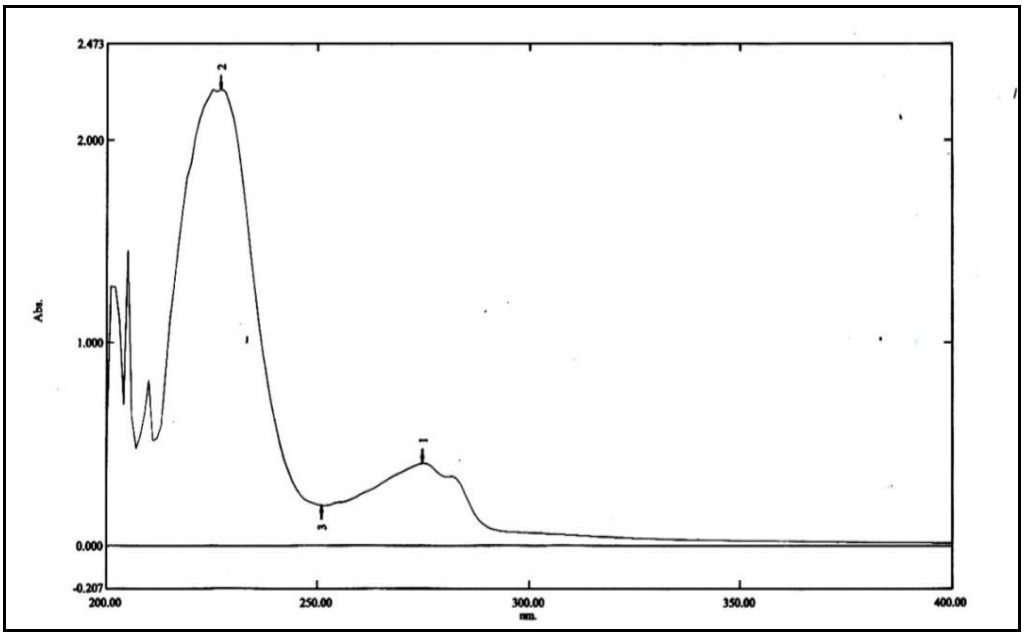

Figure No. 1: UV spectra of Aceclofenac.

Calibration Curve of Aceclofenac

Table No.5 Calibration Curve of Aceclofenac in Buffer of pH 6.8.

Sr.no	Concentration µg/ml	Absorbanceat 275nm
1	0	0.00
2	5	0.12
3	10	0.26
4	15	0.38
5	20	0.51
6	25	0.62

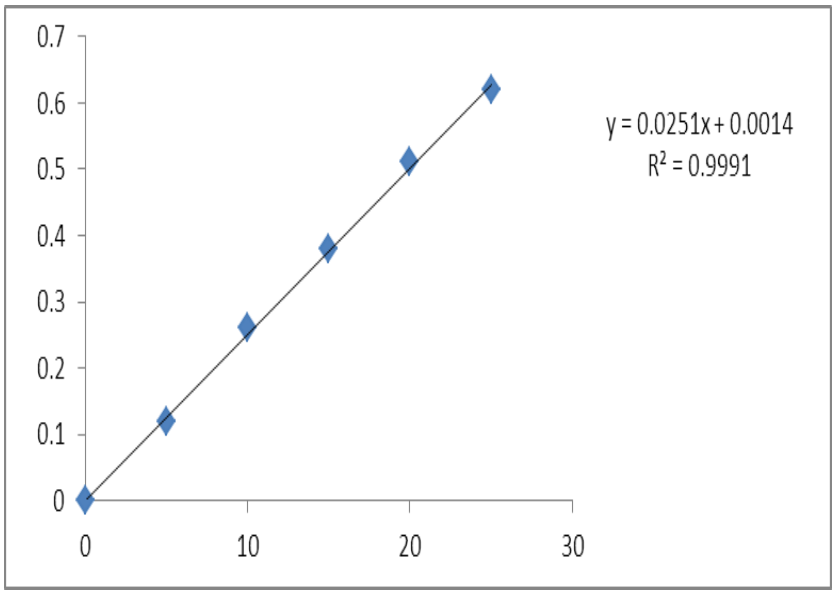

Figure no. 2: Calibration curve of Aceclofenac.

Table no. 6. Various constants for calibration curve.

Parameters	Value for calibration curve in phosphate buffer
Slope	0.025
Intercept	0.001
R^2	0.999

Excipents compatablity studies

FTIR Study

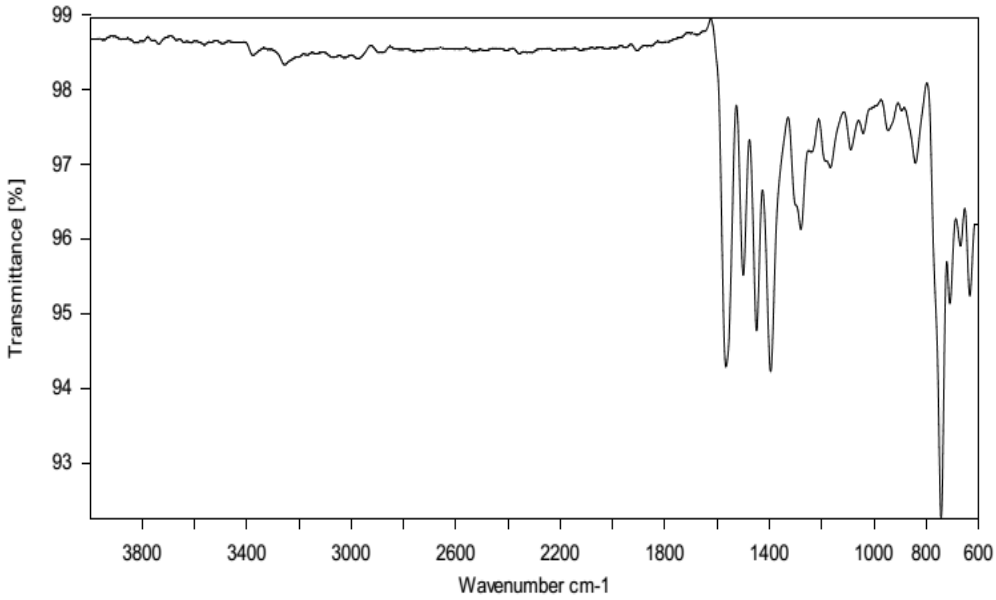

Figure no 3: FTIR Spectra of Aceclofenac.

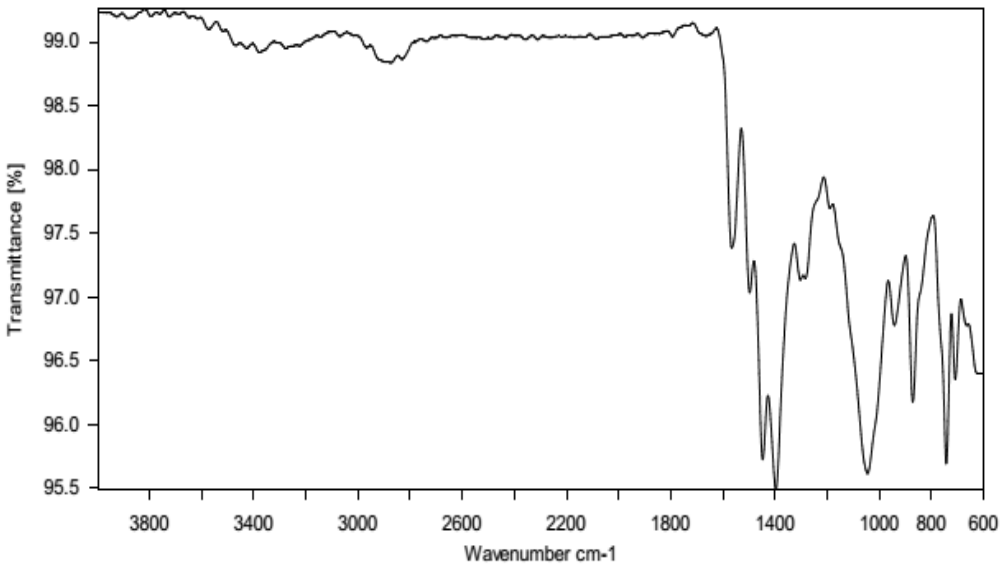

Figure no 4: FTIR Spectra of Aceclofenac+HPMC +Egg shell polymer.

Data obtained from IR Spectra

Table no.7: Interpretation of IR Spectra

IR Spectra	Peak of functional groups[Wavelength(cm^{-1})]			
	2^0 NH	Ar-C-Cl	Di Substiutional Aromatic ring	C=O group
Reference standard	1640-1550	785-540	750	1750-1730
Aceclofenac	1566	679	749	1720
Aceclofenac+ HPMC+Egg Shell powder	1565	1587	748	1721

Pre-Compression evaluations parameters

Table no.8: Flow properties of granules prepared by different techniques

Formulations	Angle of repose(θ)	Loose bulk density (gm/ml)	Tapped bulk density (gm/ml)	Percent compressibility (%)	Hausner's ratio
F1	30.96±99	0.400±0.006	0.466±0.007	13±0.47	1.15±0.015
F2	34.50±1.01	0.411±0.005	0.482±0.007	14.58±1.39	1.17±0.005
F3	34.21±1.04	0.378±0.004	0.411±0.008	9.75±0.18	1.10±0.009
F4	33.02±0.92	0.358±0.003	0.424±0.003	15.06±1.3	1.18±0.019
F5	31.79±0.20	0.341±0.001	0.424±0.003	14.04±1.05	1.16±0.004
F6	35±0.34	0.388±0.002	0.451±0.009	15.55±0.56	1.18±0.011
F7	29.68±0.14	0.368±0.001	0.411±0.004	12.19±0.004	1.13±0.020
F8	30.11±1.10	0.333±0.009	0.368±0.005	8.33±1.8	1.09±0.035
F9	26.50±1.73	0.350±0.004	0.388±0.009	7.89±0.95	1.08±0.030

Post-compression evaluations parameters

Table no.9: Evaluation of physical parameters.

Batch Code	Weight variation Average wt in (mg) ±SD	Hardness (kg/cm2) ±SD	Thickness (mm) ±SD	Friability (%)	Drug Content Uniformity (%)±SD
F1	700±3.05	4.9±0.20	4.98±0.019	0.28	98.25±1.15
F2	697±2.51	4.7±0.20	4.86±0.025	0.95	99.28±1.73
F3	702±2.00	5.2±0.10	5.00±0.01	0.88	99.68±1.00
F4	699±2.03	5.6±0.15	4.86±0.025	0.97	97.01±1.00
F5	698±1.5	5.3±0.11	4.97±0.019	0.48	99.98±1.73
F6	699±2.51	5.2±0.05	4.87±0.02	0.46	98.10±2.64
F7	701±1.52	5.8±0.17	4.98±0.030	0.48	99.72±1.15
F8	700±1.52	5.4±0.12	5.00±0.01	0.86	98±1.12
F9	699±2.00	5.6±0.15	4.97±0.019	0.47	98.12±0.07

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

In-Vitro Drug Release studies

Table no. 10: *In-vitro* Dissolution Profile of the Formulations of Direct Compression Technique (F1-F9).

Time in hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	16.92	16.56	20.08	25.56	14.94	19.44	19.26	20.34	17.1
2	18	18.36	26.28	30.06	19.44	25.2	24.48	24.3	22.86
3	20.88	21.24	29.52	35.64	23.58	35.38	30.42	30.06	29.88
4	24.3	25.2	35.1	40.68	30.06	39.6	39.96	34.92	34.74
5	28.8	28.98	39.96	42.48	38.24	48.78	48.24	42.3	41.94
6	31.14	35.28	50.76	48.96	46.26	57.96	54.72	50.58	50.04
7	34.92	40.86	54.72	51.12	53.46	64.26	64.08	58.5	58.14
8	38.7	50.4	63.72	55.26	58.32	70.56	70.5	64.98	64.26
9	43.56	55.44	70.6	59.94	63.9	74.16	74.16	70.74	71.1
10	48.24	58.56	75.24	70.56	73.8	79.92	81.54	76.5	77.4
11	49.86	64.08	76.86	73.98	79.38	81.54	86.04	82.08	85.68
12	51.48	70.74	78.66	80.46	82.44	84.78	88.02	89.1	89.46

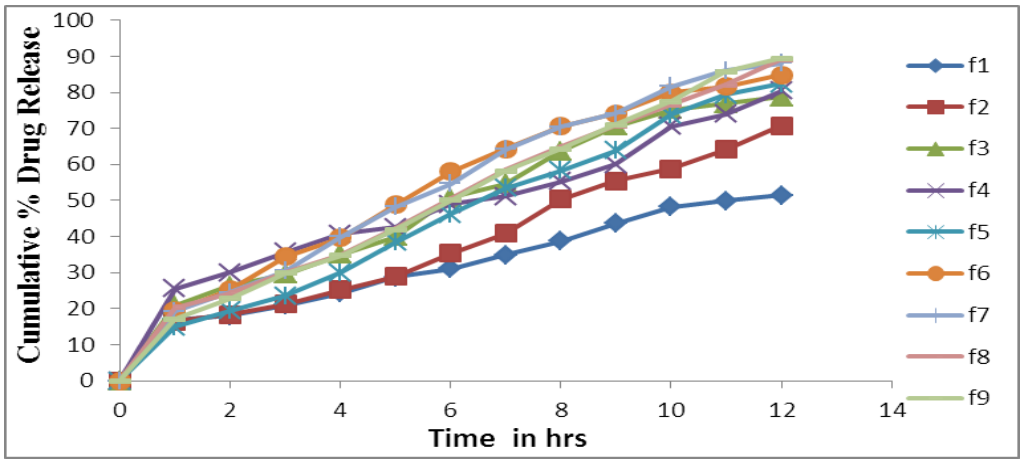

Figure no. 5: Comparative In-vitro Release Profile According to zero order kinetics for formulations F1-F9.

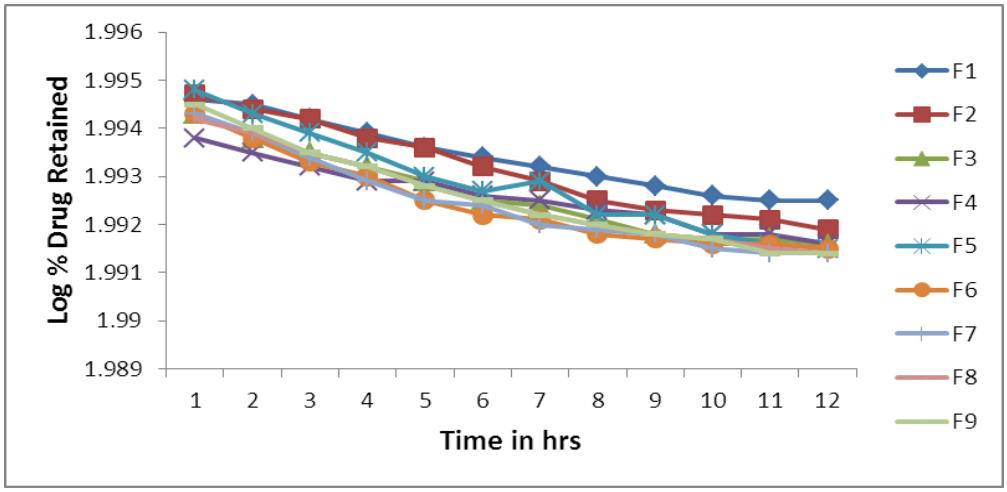

Figure no. 6: Comparative In-vitro Release Profile According to first order kinetics for formulations F1-F9.

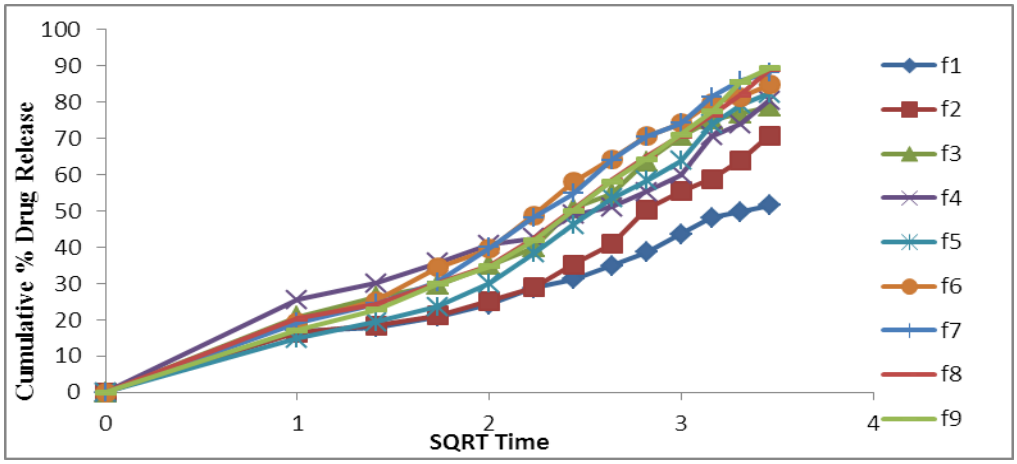

Figure no. 7: Comparative In-vitro Release Profile According to Higuchi Matrix kinetics for formulations F1-F9.

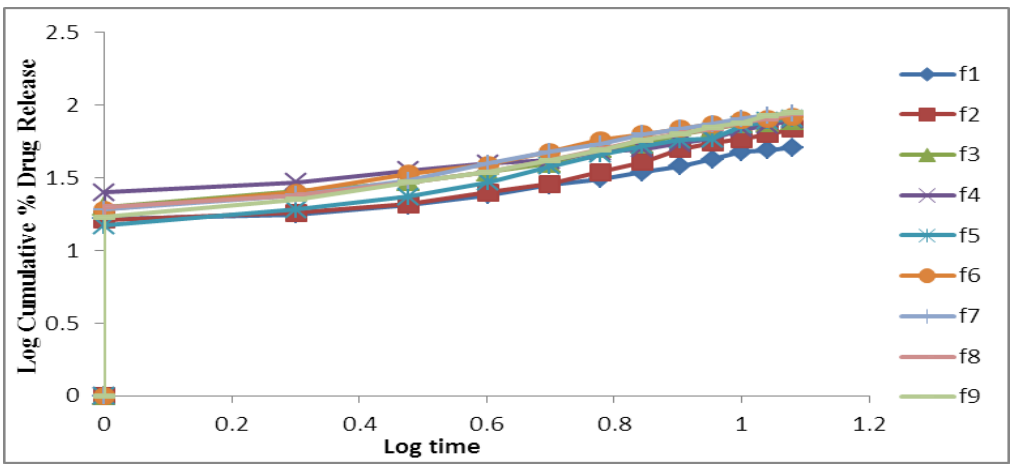

Figure no.8: Comparative In-vitro Release Profile According to Korsmeyer Peppas kinetics for formulations F1-F9.

Kinetic Data

Table no.11: Drug release kinetic model.

Formulation Code	Zero-order	First-order	Higuchi Model	Peppas Model	Best Fit Model
F1	0.960	0.976	0.969	0.643	First order
F2	0.982	0.979	0.923	0.704	Zero order
F3	0.968	0.955	0.964	0.665	Zero Order
F4	0.942	0.981	0.967	0.582	First order
F5	0.993	0.963	0.940	0.744	Zero order
F6	0.966	0.905	0.980	0.681	Higuchi
F7	0.978	0.937	0.970	0.694	Zero order
F8	0.986	0.968	0.957	0.684	Zero order
F9	0.992	0.956	0.953	0.717	Zero order

Stability Study Data

Table no.12: Stability study data.

Time	Evaluation parameters				
	Colour	Hardness (kg/cm^2)	Drug content Uniformity (mg)	% CDR	Thickness (mm)
After 1 month	white	5.6±0.07	98.04±0.05	87.27	4.97±0.15

DISCUSSION

Preformulation Studies

Melting point

The melting point of Aceclofenac was determined by capillary tube method and it was found to be 149^0C. This value is same as that of literature value.

Solubility

The Aceclofenac is freely soluble in acetone, soluble in methanol, ethanol, insoluble in water

UV Scanning

In Figure 6.1 observed that the drug was shown maxima at 275nm in phosphate buffers pH 6.8.

Standard calibration curve of Aceclofenac

Standard solution

Weight of Aceclofenac taken = 100mg, Volume made up to 100 ml Concentration of standard solution = 1 µg/ml.

Working standard solution

Weigh accurately 1mg of Aceclofenac and dissolve in 5ml of methanol and made upto 100ml with phosphate buffer pH 6.8 in a standared flask to get 10ug/ml solution. Then the solution was serially diluted to get 5, 10, 15, 20, 25µg/ml stock solution and the λmax of the stock was find out. The absorbance of the solution was measured in a UV spectrophotometer at 275nm. A calibration curve was plotted by taking concentration of the solution in ug on X-axis and absorbance on Y-axis and co-efficient "r" was calculated.

The linear regression analysis for standard curve

For standard curve in phosphate buffer pH 6.8 the linear regression analysis was done on Absorbance data points. The results are as follows;

The slope = 0.025

The intercept = 0.001

The correlation coefficient = 0.99

Compatibility study of Pure Drug and polymers

The infrared spectral analysis of the procured Aceclofenac was carried out. Sample was compared with the reference standard IR spectrum of Aceclofenac. The IR spectrum was measured in the solid state as potassium bromide dispersion. The IR spectrum of Aceclofenac is presented in Figure.1 and Observed peaks are shown in Table.no.7; these peaks are similar to reported peaks of Aceclofenac. Physical mixture of drug and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference in the functional groups as the principle peaks of the Aceclofenac were found to be unaltered in the spectra of the drug-polymer physical mixture shown in figure no.4. Comparisons of peaks of different functional groups are tabulated in Table no.7.

Pre-compression parameters

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study the flow properties of granules, to achieve uniformity of tablet weight. Angle of Repose, Loose Bulk Density, Tapped Bulk Density and Carr's Compressibility Index:

Angle of repose (θ)

The data obtained for angle of repose for all the formulations were tabulated in Table no.3 and bar graph comparison was shown in table no.3 The values were found to be in the range of $26^{o}50'$and $35^{o}'$. All the formulations prepared by both the methods showed the angle of repose less than 35^{0}, which reveals good flow property.

Bulk density

Bulk density for all the formulations batches varied from 0.333gm/cm^3 to 0.411gm/cm^3. The result lies within the acceptable range and this result helps in calculating the percent Compressibility of the powder. In optimized batch the bulk density should within limit so depending upon that, we can conclude that formulation have good flow property.

Tapped density

Tapped density for all the formulation batches varies from 0.368gm/cm^3 to 0.482gm/cm^3. The values obtained lies within the acceptable range and not large differences found between tapped densities. This result helps in calculating the % compressibility of powder. In optimized batch the tapped density should within limit so depending upon that, we can conclude that formulation have good flow property.

Carr's consolidation index

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 8.33 to 15.08. The directly compressible granulations had shown excellent compressibility index values up to 15% result in good to excellent flow properties. The results for all the formulations were shown in Table no 9.

Hausner's ratio

The Hausner's ratio for all the formulation batches lies within the range of 1.08 to 1.18. The values obtained lies within the acceptable range and not large difference found. All formulation was shows good flow abilities. In optimized batch the hausner's ratio should be within limit i.e. below 1.18 so depending upon that, we can conclude that formulation has good flow property.

Formulation design

The present study was carried out to develop Aceclofenac sustained release matrix tablets in order to improve patient compliance and also to prepare used eco-friendly formulation.

In this case, nine formulations of sustained release matrix tablets were prepared using polymer HPMC, Egg shell powder in different ratio. The detailed composition of each formulation is given in the Table no 1.

Post compression parameters

The tablets prepared by direct compression technique was subjected for evaluation according to various official specifications and other parameters like, shape, thickness, hardness, friability, weight variation, drug content, *in-vitro* dissolution studies, model fitting of release profile, for tablets formulated by direct compression method and stability studies.

Shape, Diameter and color of tablets

Formulations prepared, were randomly picked from each batch examined under lens for shape and in presence of light for colour. Tablets showed 12mm diameter, flat, circular shape in white colour.

Thickness

Thickness of the tablets was measured by vernier caliper by picking tablets randomly from all the batches. The results of thickness for tablets were shown in Table no.6.5. The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 4.86 mm to 5 mm. The standard deviation values indicated that all the formulations were within the range.

Hardness

The hardness of all the tablets prepared by direct compression method was maintained within the 4.7 kg/cm^2 to 5.9 kg/cm^2. The mean hardness test results are tabulated in Table no.9. The hardness values ranged from 4.7 kg/cm^2 to 5.9 kg/cm^2 for formulations were almost uniform.

Friability test

The study results were tabulated in Table no.9 and were found to be well within the approved range (<1%) in all designed formulations. The formulations F6 showed slightly higher than the other. The values were found to be within the limit. Thus tablets possess good mechanical strength.

Weight variation test

The weight variation for all the formulations is shown in Table no 9. All the tablets passed weight variation test as the average percentage weight variation was within the

pharmacopoeial limits of 5%. It was found to be 697 mg to 702 mg. The weight of all the tablets was found to be uniform with low standard deviation.

Drug Content

The drug content uniformity was performed for all the nine formulations and results are tabulated in Table 9.Three trials from each batch were analyzed spectrophotometrically. The average value and standard deviations of all the formulations were calculated. The drugs content of the tablets were found to be between 98.25 to 98.12 of Aceclofenac.

***In-vitro* Dissolution Study**

All the nine formulations were subjected for *in-vitro* dissolution studies using USP type 2 Dissolution test apparatus (USP XXIIII). The dissolution medium 6.8 pH buffer was used to study the drug release. The samples were withdrawn at different intervals of time and analyzed at 275nm using UV spectrophotometer. Cumulative percentage drug release was calculated on the basis of amount of Aceclofenac present in the respective formulations. The data obtained in the *in-vitro* release for formulations prepared by direct compression technique are tabulated in the Table no 10. The plots of cumulative percentage of Aceclofenac released as a function of time (t) for formulations prepared by direct compression technique (F1 to F9) are shown in Figure No.5

All the formulations showed % drug release (51.48% - 89.46%). Formulations F1, F2, F3, F4, F5 F6, F7, F8 and F9 showed 51.48%, 70.74%, 78.66%, 80.46%, 82.44%, 84.78%, 88.02%, 89.1%, 89.46, of drug release respectively. But the slow drug dissolution was noticed in F9 formulation compared to other formulations, which releases at the end of 12 hours.

Stability studies

Stability studies of optimized formulation F_9

Stability studies for the developed formulations were carried out by storing the selected formulations at 40°C/75% RH up to one month. The formulation F9 was selected on the basis of their high cumulative percentage drug release. After one month, the tablets were analyzed for the colour, hardness, drug content uniformity and cumulative % drug released. These formulations showed no significant changes in the values. The data obtained are tabulated in Table no.12 From the obtained data of tablet evaluation parameters indicated that stable formulations can be developed using direct compression method.

CONCLUSION

The result of the present study demonstrated that the HPMC and Egg shell powder were used as a drug release retardant and drug release was dependent on polymers proportion. The drug release was extended over a period of 12 hours and the to be good without capping and chipping.

- The present investigation described the influence of concentration of polymer (HPMC & Egg shell powder) on Aceclofenac release.
- The in-vitro dissolution profiles of all the prepared Aceclofenac sustained release matrix tablet formulations were found to extend the drug release over a period of 10 to 12 hours.
- IR spectroscopic studies indicate no drug- excipients interaction in the prepared formulations.
- Comparing the all formulations, sustained release formulation of F9 was considered as optimized formulation which exhibited 89.46 % of drug release in 12 hours.
- From the result it was observed that drug and polymer ratio influence the in vitro drug release of Aceclofenac sustained release matrix tablets. Hence, the sustained release matrix system of Aceclofenac is expected to provide Clinician with a new choice of safe and more bioavailable formulation in the management of inflammation.

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