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# DEVELOPMENT AND ASSESSMENT OF MATRIX TABLETS OF ACECLOFENAC EMPLOYING HYDROPHILIC POLYMERS

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## ABSTRACT

Aceclofenac is an anti-rheumatic and non-steroidal anti-inflammatory medicine (NSAID) utilized to cure an extensive assortment of painful conditions (e.g., arthritis, gout, lupus, sciatica, back pain, traumatic pain, gynecological pain, etc.) with minimal and infrequent adverse effects. Its biological half-life, however, is only 4–4.3 h. So, to have a longer-lasting effect, you need medication with a controlled release. Aceclofenac requires a loading dosage of a lower dose and a maintenance dose of a higher dose. Since its therapeutic effect can be extended by using sustained-release matrix tablets, it is a medication of choice for this purpose. In the current research, hydrophilic polymers (HPMC, Carobopol 940) were utilized to prepare and evaluate matrix tablets of aceclofenac, in the hope of achieving sustained drug release after a single dose has been given, hence extending the drug's therapeutic effect. The FTIR analysis showed that the medicine is completely compatible with all of the excipients used in the formulation. This approach of direct compression was preferred to create the tablets. The tablets were examined for hardness, thickness, weight fluctuation, Content Uniformity, friability, swelling index, and in-vitro release. All of the tablets had qualities that could be considered satisfactory. With an average G.I. residence length of 10–12 hours, our matrix formulation containing [HPMC and Carbopol 940 (75:25)] is possibly demonstrating superior release.

**Keywords: NSAID; Matrix tablets; Aceclofenac; HPMC; Carbopol 940**

## INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are generally considered first-line therapy for the symptomatic management of joint pain, osteoarthritis, and ankylosing spondylitis. When it comes to non-steroidal anti-inflammatory drug (NSAID) molecules, aceclofenac is on the rise as a potential treatment for arthritis. Matrix tablets have several applications in medicine, particularly for long-term dosing. Inadequate drug adherence occurs when patients have trouble swallowing pills and tough gelatin capsules **[1-3]**. Recent innovations in drug delivery methods have been made to improve patient compliance and, by extension, the safety and efficacy of the therapeutic molecule. Some people, especially children, the elderly, the unconscious, and those confined to beds, have trouble swallowing regular tablets or capsules and therefore benefit greatly from rapid dissolving tablets. To get over this problem, scientists created fast-dissolving and dispersible tablets **[4-6]**. Freeze drying/lyophilization, tablet moulding, and direct compression are the most frequent procedures used to create these tablets. Lyophilized tablets have a porous structure, allowing saliva to quickly enter the pores upon placement in the oral cavity; nonetheless, the production method is expensive **[7-10]**.

The most effective therapeutic response is often seen with many medications simply after stable blood levels are reached furthermore maintained. Sustained-release dose forms are ideal for medications with a biological half-life of 3-4 h **[11-12]**. Thus, an SR formulation of this medication is appropriate for administration. Aceclofenac, when taken for an extended period of time, may be effective at a lower, once-daily dose. For more potent non-steroidal anti-inflammatory action is needed, the recommended dose can be increased to 200 mg TDS. Common maintenance dosing schedules call for 200 milligrams (mg) daily, split into two doses of 100 mg each, taken 12 h apart (i.e., when you get up and again before bed). Treatments can be given at regular 12 h intervals if desired. Depending on how severe your arthritis is, you may need to alter both your morning and evening doses **[13-15]**.

The purpose of the current research is to determine how to maintain a therapeutically effective and non-toxic blood or tissue level for an extended duration of time. The aspiration of sustained-release drug delivery systems is to treat a wide variety of

acute and chronic diseases with fewer adverse effects and fewer drug doses per day than is now the case **[16-18]**.

## MATERIALS AND METHODS

Lupin Pvt. Ltd. of Aurangabad generously provided a sample of their Aceclofenac drug for our testing. We shopped at Research Lab in Mumbai for our carbopol 940, magnesium stearate, and microcrystalline cellulose. The HPMC, starch, talc, and lactose were all of analytical grade and sourced from various distributors.

### Pre-formulation study

### Melting point

Aceclofenac melting point was measured using Thiele's tube melting point equipment, which required only a tiny sample to be deposited in a capillary tube at one end. Triplicate measurements were taken of the melting point.

### Solubility

Phosphate buffer at pH 7.4 and sterile water were used to test the drug's solubility. After removing extra medication, 10 ml of the solvent was added to the empty 30 ml glass vial. After 30 minutes of sonication, the vials were left alone for 24 hours to allow for equilibrium. The absorbance of the diluted solutions was evaluated using a UV spectrophotometer at 274 nm after 24 hours of exposure to the saturated solution via a filter.

### Selection of wavelength

Maximum absorption was observed at 274 nm after examining a solution of Aceclofenac in phosphate buffer pH 7.4 from 200 to 400 nm using a shimadzu 1800 UV spectrophotometer and a 1 cm quartz cell.

### UV spectroscopy

A 100-milligram dose of Aceclofenac was measured out and poured into a volumetric flask. A stock solution of 1000 g/ml was obtained by dissolving it in phosphate buffer at pH 7.4 and bringing the volume up to 100 ml. Concentrations ranging from 5 g/ml to 30 g/ml were achieved by drawing off aliquots and diluting them with water. We used spectrophotometry to determine the absorbance of the solution at 274 nm.

### Fourier transforms infrared spectroscopy (FTIR)

Triturating a dry Aceclofenac sample with a dry potassium bromide (A.R. Grade) sample, the mixture was then deposited in a sample cell. It was determined by recording and analyzing the infrared spectrum of the medication sample.

### Preparation of sustained release matrix tablets of Aceclofenac

In **Table 1** you can see the individual ingredients that make up each pill. Aceclofenac, pure HPMC, carobopol 940, MCC, lactose, and starch were all combined together in a glass mortar and pestle using their respective weighed amounts to get a consistent consistency. After that, 1% w/w of both magnesium stearate and talc were added as lubricants and mixed in a Polybag. At last, the mixture was compressed in a Rimek tablet compression machine using 12 mm round shaped punches to yield 500 mg weight tablets. Multiple criteria were used to assess the effectiveness of the resulting matrix tablets.

**Table 1: Composition of matrix tablet of Aceclofenac**

| Ingredients(mg) | Code of Formulation | | | | |
|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 |
| Aceclofenac | 200 | 200 | 200 | 200 | 200 |
| Pure HPMC | 100 | 75 | 50 | 25 | - |
| Carbopol 940 | - | 25 | 50 | 75 | 100 |
| Microcrystalline Cellulose | 25 | 25 | 25 | 25 | 25 |
| Starch | 75 | 75 | 75 | 75 | 75 |
| Lactose | 90 | 90 | 90 | 90 | 90 |
| Magnesium Sterate | 5 | 5 | 5 | 5 | 5 |
| Talc | 5 | 5 | 5 | 5 | 5 |
| Total weight (mg) | 500 | 500 | 500 | 500 | 500 |

**Evaluation of pre-compression properties/ powder blend**

**Angle of repose**

Powder mix flow properties were characterised by measuring the angle of repose using the fixed height method. Two centimetres above the base, a funnel with a stem diameter of 10mm was affixed. The sample was carefully moved up the inside of the funnel until the top of the resulting pile touched the top of the funnel. The powder cone's radius was determined by drawing a crude circle around the pile's base.

**Bulk Density**

All samples' bulk densities were calculated by passing the samples through with a glass funnel together into 100 ml graduated cylinder. The sample's volume was measured. There was a determination of bulk density.

**Tapped density**

Pouring material through a glass funnel into a 100 ml graduated cylinder gave us the tapped density. The volume of the cylinder was held constant by tapping it from a height of 2 inches. Recording the sample's volume and then calculating its tapped density.

**Compressibility Index**

Powder flow properties can be

predicted quickly and easily using the compressibility index or its close relative, Hausner's ratio. Both the bulk density and the tapped density of powder are used to calculate the compressibility index and Hausner's ratio, respectively. **Table 2** provides a ranking of the powders based on their Carr's index flow qualities.

**Hausner's ratio**

The tapped density over bulk density ratio.

**Post -compression properties**

**Appearance**

Tablets were examined visually for signs of capping, chipping, including lamination.

**Tablet Dimensions/ Thickness**

A Vernier Caliper, properly adjusted, was used to measure the thickness and the diameter. In order to determine the average thickness of the tablets, we choose 5 at random from each formulation and measured them manually.

**Hardness**

Despite the lack of an official hardness test, tablets should be handled adequately during shipping and storage. A computerized hardness tester was used to determine the tablet's level of toughness. The force necessary to crack tablets that have been arranged at an acute angle to one other. There were five tablets tested from each batch, and the average of the three readings was used to determine the hardness of the tablets (in $kg/cm^2$).

**Weight Variation Test**

Each pill is weighed separately before the mean is computed and compared to the IP weight variation test mean. Granulation and mechanical issues are the two main sources of weight variance. The dies won't be filled evenly if the granule size is too big. Low punches of varying lengths might also be the source of mechanical issues.

**Friability**

Friction and shocks can cause tablets to chip, cap, or break; hence a friability test is used to evaluate their impact. The Roche friabilator was used to measure the brittleness of the pills. Percentages are used to show the value. After initially Weighing (W initial) 20 pills, they were moved into the friabilator. The friabilator was run at 25 rpm for 4 minutes, and it was eventually increased to 100 rpm. After reweighing the tablets (Wfinal). Having a tablet friability percentage of less than 1% was regarded satisfactory. Next, we determined the percentage of friability.

**Uniformity of drug content**

Five tablets of each formulation were weighed, crushed in a mortar, and the

resulting powder was mixed in 50 ml of methanol to yield 50 mg of Aceclofenac. Phosphate buffer was used to bring the volume of this stock solution down from 100 ml to 2 ml (pH7.4). Using a double beam UV-Visible spectrophotometer, the absorbance was determined to be 274 nm.

**Swelling Index**

Tablets were stored in a 7.4 pH buffer solution for 12 hours on a Petri dish. After 1 hour, each tablet was removed, soaked in water, and weighed to observe its swelling behaviour.

**In-vitro drug release studies**

An in vitro drug availability test should theoretically quantify the physical phenomenon influencing availability in vivo. As the content of gastrointestinal fluids varies, and the dosage form passes through the fluids at a rate that is not known, this is not possible for orally delivered dose forms. There is no way to model a single test system that would account for all factors, including drug-component interactions, volume shifts, retention times, transit times, and agitation levels. However, in vitro testing can show how these factors influence the rate and pattern of drug release from a given dose form. This will help predict how the dosage form will perform in future in-vivo experiments. Using a USP paddle type II model dissolution test apparatus, in vitro dissolving tests were conducted in a phosphate buffer (pH 7.4) to mimic the digestive system.

**Particulars of dissolution test are as follows:**

| Dissolution test apparatus | USP Type II |
|---|---|
| Speed | 50 RPM |
| Volume of medium | 500 ml |
| Sample withdrawn | 5 ml |
| Medium used | Phosphate buffer (pH 7.4) |
| Temperature | 37 ± 0.5 °C |

**Curve fitting analysis**

Data were plotted as follows to examine the mechanism of the dosage form's drug release rate kinetics:

1. The cumulative percentage of drugs released over time (In-Vitro drug release plots)
2. Cumulative proportion of drug release vs. square root of time (Higuchi's plots).
3. Cumulative drug proportion log versus time (First order plots)
4. Log time versus log percentage of medication released (Peppas plots)

## RESULTS AND DISCUSSION

### Melting point

The melting point, measured in triplicate, was determined to be between 148 and 150 degrees Celsius, which are in accordance with pharmacopoeial requirements.

### Solubility study

Aceclofenac has a solubility of 5.53 1.2337 mg/ml in a phosphate buffer at a pH of 7.4, but it is almost completely insoluble in purified water.

### UV spectroscopy

Its ultraviolet spectrum is depicted in **Figure 1** below. Maximum absorbance (max) at 274 nm was measured in a pH 7.4 phosphate buffer.

### Fourier transforms infrared spectroscopy (FTIR)

An FTIR study confirmed that the drug was safe to use in combination with all of the excipients **(Figure 2)**.

### Evaluation of pre-compression parameters

It has been determined that all five formulations are compressible because the Carr's Compressibility index is less than 17%. Both the bulk density and Tapped density of all the formulation powders were determined to be less than 1. Powders of all formulations were found to be easily compressible and had a high degree of fluidity, according to examinations of repose angles **(Table 2)**.

### Physical and chemical properties of the finished product are assessed

Preliminary characterization was performed on the produced tablets, including measurements of hardness, thickness, weight fluctuation, friability, and drug content. Evaluation investigations showed that all eight formulations fell within the range of values allowed by the pharmacopoeia for the various parameters measured. **Table 3** summarises the numerical data.

The tablets were subjected to in-vitro release, swelling index, hardness, thickness, weight variation, content uniformity, and friability tests. Everything came back good, as expected.

### Swelling Index (Table 4, Figure 3)

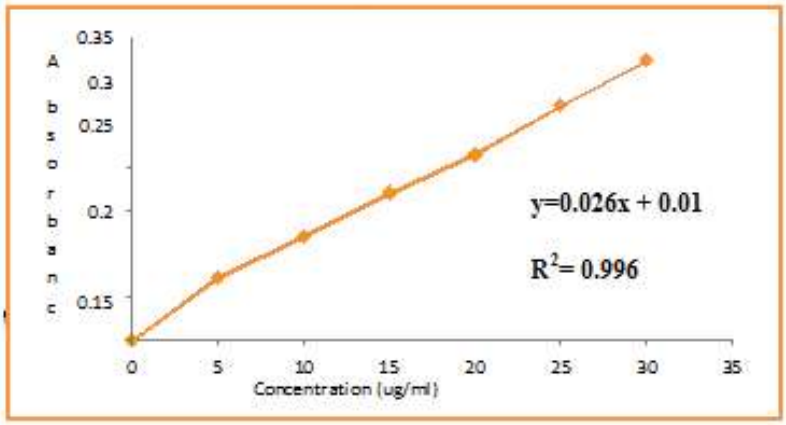
Both matrix swelling and solvent penetration have significant effects on tablet dissolution. All the results of swelling index favor the matrix tablet formulations with sustained effect **(Table 5)**.

Sustained-release aceclofenac matrix tablet compositions showed a steady, preferable release profile. Within 12 hours, which is the typical G. I. residence time, 98.34% of the drug is released, suggesting our matrix formulation, which consists of

HPMC and Carbopol 940 in the ratio of 75:25, has better release **(Figure 4)**.

**Kinetic modeling**

Curve fitting revealed that the zero order models and the Higuchi model provided the greatest fit for the in-vitro release kinetics of all formulations. When n is more than 0.5, it's possible that Aceclofenac is released via a method other than diffusion **(Table 6)**.



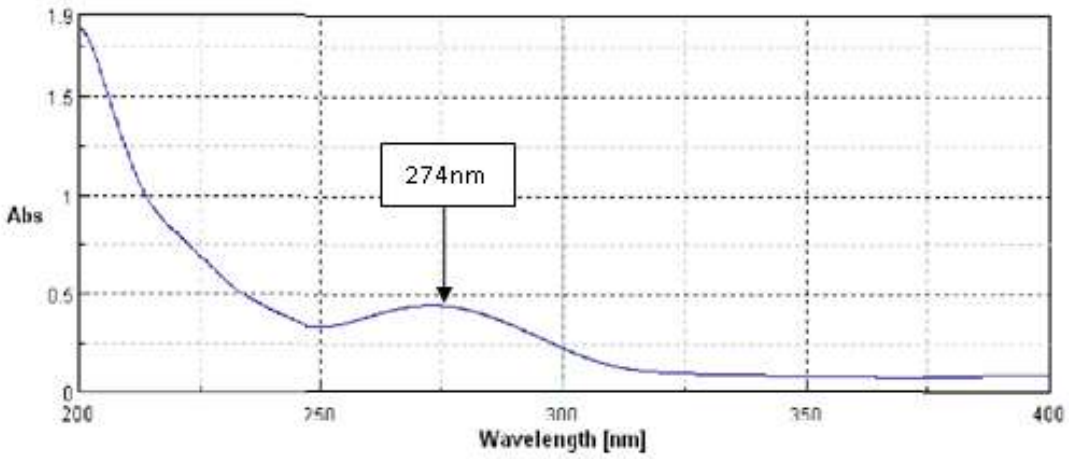




**Figure 1: Standard Curve of Aceclofenac**

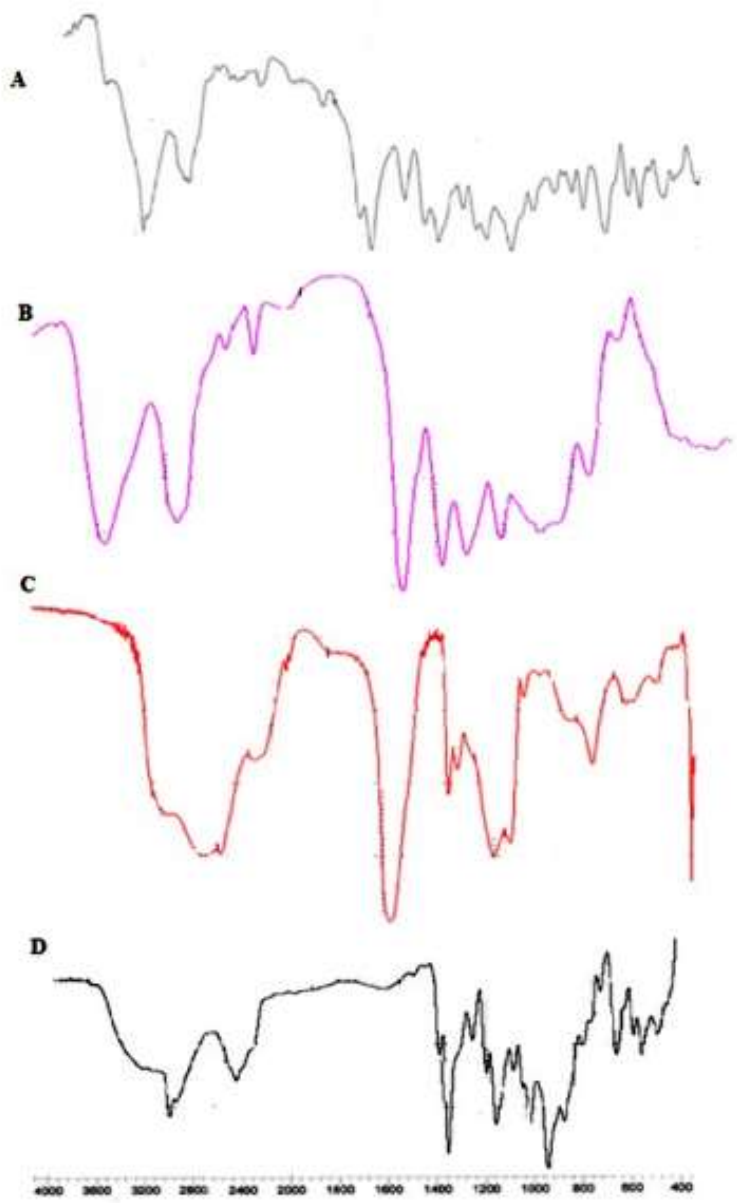



**Figure 2: IR Spectra of Aceclofenac (A), HPMC (B), Carbopol 940 (C) and Matrix Tablet (D)**

**Table 2: Aceclofenac matrix tablet pre-compression evaluation**

| Formulation | Angle of Repose (θ) | Loose Bulk Density (LBD) (g/ml) | Tapped Bulk Density (TBD) (g/ml) | Carr's Compressibility Index (%) | Hausner ratio* |
|---|---|---|---|---|---|
| F1 | $27^0.22'$ | 0.495 | 0.576 | 14.06 | 1.16 |
| F2 | $27^0.10'$ | 0.478 | 0.539 | 11.31 | 1.12 |
| F3 | $29^0.45'$ | 0.470 | 0.536 | 12.31 | 1.14 |
| F4 | $32^0.56'$ | 0.465 | 0.566 | 17.84 | 1.21 |
| F5 | $31^0.42'$ | 0.465 | 0.577 | 16.51 | 1.24 |

Table 3: Evaluation of post-compression parameters of matrix tablets ofAceclofenac

| Formulation code | Thickness (mm) | Hardness ($Kg/cm^{2)}$ | Weight Variation (mg) | Friability(%) | Drug Content Uniformity (%) |
|---|---|---|---|---|---|
| F1 | 4.4 | 5.9 | 500 | 0.63 | 99.85 |
| F2 | 4.7 | 6.8 | 502 | 0.54 | 100.2 |
| F3 | 4.3 | 6.1 | 505 | 0.72 | 99.45 |
| F4 | 4.7 | 5.7 | 501 | 0.51 | 98.29 |
| F5 | 4.5 | 6.2 | 507 | 0.67 | 99.42 |

*All Values are expressed as mean ± SD, n=5.

Table 4: % Swelling index of all formulations

| Time (h) | % Swelling index | | | | |
|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 |
| 1 | 41.23 | 36.34 | 37.77 | 44.02 | 47.02 |
| 2 | 52.82 | 44.48 | 51.96 | 59.85 | 64.85 |
| 3 | 68.71 | 61.84 | 69.03 | 74.71 | 76.71 |
| 4 | 83.05 | 78.69 | 86.93 | 84.07 | 86.05 |
| 5 | 96.19 | 93.56 | 98.97 | 95.19 | 103.9 |
| 6 | 119.6 | 112.5 | 124.4 | 117.6 | 121.6 |
| 7 | 132.0 | 131.8 | 139.9 | 134.2 | 137.1 |
| 8 | 156.5 | 145.9 | 164.4 | 151.3 | 170.2 |
| 9 | 167.4 | 164.3 | 178.8 | 164.4 | 186.4 |
| 10 | 187.3 | 179.1 | 187.1 | 185.3 | 195.3 |
| 11 | 208.1 | 195.2 | 212.9 | 204.5 | 206.5 |
| 12 | 221.0 | 217.1 | 223.0 | 219.0 | 237.0 |

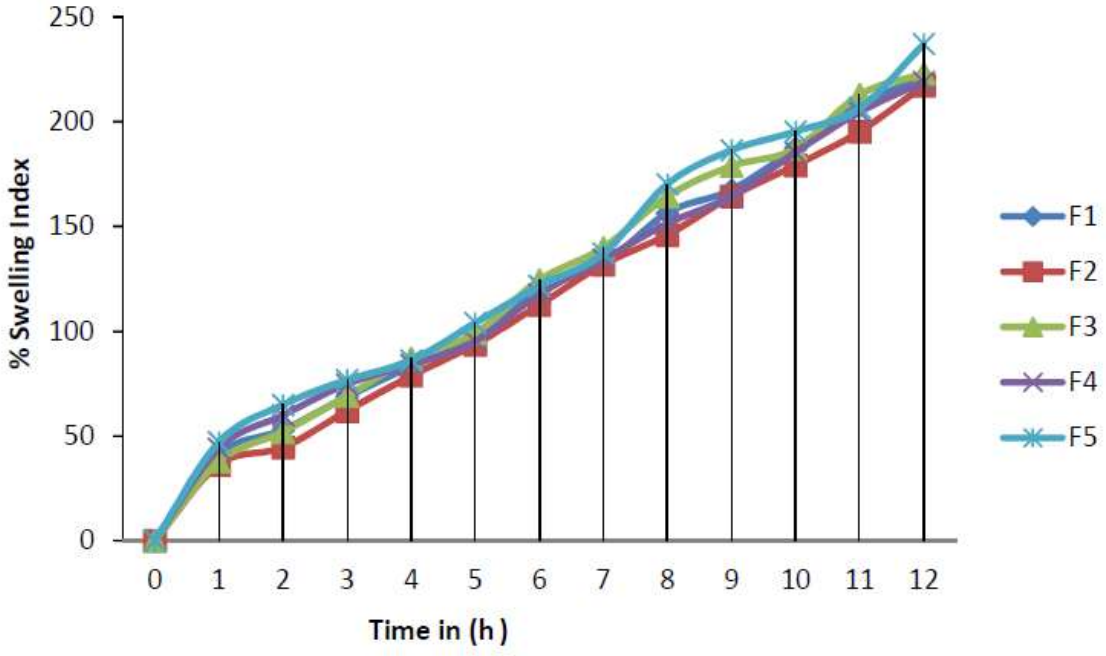



Figure 3: % Swelling index of F1 to F5

**Table 5: In-vitro drug release of formulation F2**

| Time (h) | Square Root of Time | Log Time | Cumulative percentage Drug Release | Cumulative percentage Drug Remain | Log Cumulative percentage Drug Release | Log Cumulative percentage Drug Remain |
|---|---|---|---|---|---|---|
| 1 | 1.000 | 0.000 | 24.7 | 75.3 | 1.392 | 1.876 |
| 2 | 1.414 | 0.301 | 29.95 | 70.05 | 1.476 | 1.845 |
| 3 | 1.732 | 0.477 | 37.2 | 62.8 | 1.570 | 1.797 |
| 4 | 2.000 | 0.602 | 44.21 | 55.79 | 1.645 | 1.746 |
| 5 | 2.236 | 0.698 | 51.23 | 48.77 | 1.709 | 1.688 |
| 6 | 2.449 | 0.778 | 58.67 | 41.33 | 1.768 | 1.616 |
| 7 | 2.645 | 0.845 | 66.45 | 33.55 | 1.822 | 1.525 |
| 8 | 2.828 | 0.903 | 74.13 | 25.87 | 1.869 | 1.412 |
| 9 | 3.000 | 0.954 | 82.32 | 17.68 | 1.915 | 1.247 |
| 10 | 3.162 | 1.000 | 86.57 | 13.43 | 1.937 | 1.128 |
| 11 | 3.316 | 1.041 | 90.63 | 9.27 | 1.957 | 0.967 |
| 12 | 3.464 | 1.079 | 98.34 | 1.66 | 1.992 | 0.220 |

***Each reading is an average of three determinations**

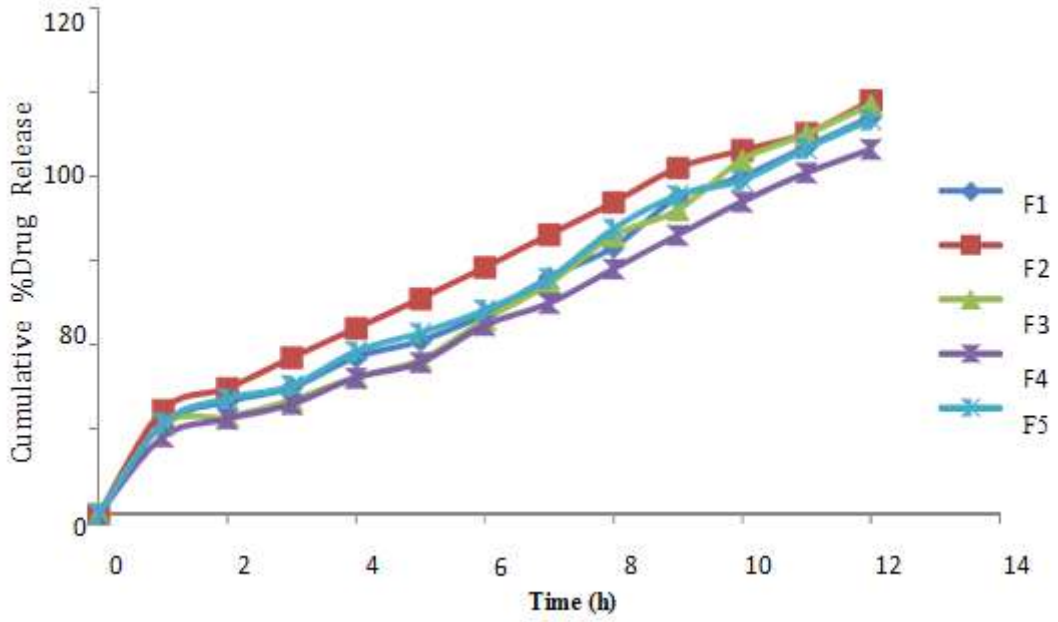



**Figure 4: *In-vitro* dissolution profile of F1 to F5 formulation**

**Table 6: Kinetics data obtained from in-vitro release profile for matrix tablets of Aceclofenac**

| ormulationcode | Zero-order kinetics | First-order kinetic | Huguchi | Peppas | |
|---|---|---|---|---|---|
| | $R^2$ | $R^2$ | $R^2$ | $R^2$ | n-value |
| F1 | 0.983 | 0.849 | 0.971 | 0.931 | 0.737 |
| F2 | 0.976 | 0.812 | 0.996 | 0.991 | 0.699 |
| F3 | 0.944 | 0.792 | 0.986 | 0.960 | 0.844 |
| F4 | 0.982 | 0.877 | 0.978 | 0.973 | 0.809 |
| F5 | 0.989 | 0.876 | 0.987 | 0.977 | 0.743 |

## CONCLUSION

Sustained-release Aceclofenac can prevent unwanted peaks in blood plasma active concentration. In this study, a sustained-release Aceclofenac formulation is created. Controlling medication release usually involves a matrix approach. Polymer matrix technologies are often employed in prolonged medication administration to optimise drug release and regulatory acceptability. This study aims to generate twice-daily sustained-release Aceclofenac matrix tablets using HPMC and Carobopol 940. F2 formulation uses hydrophilic polymers HPMC and Carbopol 940 in a 75:25 ratio to enable slow and sustained release over 12 h. Slowing medication release and building a matrix were successful. The zero order model and the Higuchi model best fit the in-vitro release kinetics of all formulations, as indicated by curve fitting. $n > 0.5$ suggests non-fickian transport may follow diffusion as aceclofenac's release mechanism. 98.34% of the drug is released within 12 h, which is the usual G. I. residence length, suggesting our matrix formulation, which comprises HPMC and Carbopol 940 in the ratio 75:25, has better release.

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