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# FORMULATION AND INVITRO EVALUATION OF CEFPROZIL SUSTAINED RELEASE TABLETS BY USING SYNTHETIC POLYMERS

**Gollapudi Rajesh[1*], Azmeera Ramarao[2], Paladugu Sujitha[3], Md Parveen [4]**

[1]Department of Pharmaceutics, Max Institute of Pharmaceutical Sciences, Khammam, Telangana, India.
[2]Department of Pharmaceutical Analysis, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India.
[3]Department of Pharmaceutical Analysis, Max Institute of Pharmaceutical Sciences, Khammam, Telangana, India.
[4]Department of Pharmaceutics, Max Institute of Pharmaceutical Sciences, Khammam, Telangana, India.

**ABSTRACT**

The aim of the present study was to develop sustained release formulation of Cefprozil to maintain constant therapeutic levels of the drug for over 12 hrs. Various natural polymers such as Guar gum, karaya gum and locust bean gum were employed as polymers. Cefprozil dose was fixed as 500 mg. Total weight of the tablet was considered as 750 mg. Polymers were used in the concentration of 62.5 mg and 125 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

**Key words:** Cefprozil, Guar gum, Gum karaya and Sustained release tablets.

## INTRODUCTION

The treatment of acute diseases or chronic illness has been achieved by delivery of drugs through different drug delivery systems such as tablets, injectables, suspensions, creams, ointments, liquids and aerosols. Another role of the delivery systems is to allow the safe application of the drug. This includes that the drug in the formulation must be chemically, physically and microbiologically stable. Side-effects of the drug and drug interactions should be avoided or minimised by the use of suitable drug delivery systems. The delivery systems also need to improve the patient's compliance with the pharmacotherapy by the development of convenient applications. Finally, the delivery system needs to be reliable and its formulation needs to be technically feasible [1-10]. This means the pharmaceutical quality of the delivery systems needs to be assured, drug release from the system needs to be reproducible and the influence of the body on drug release should be minimized. The ultimate goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration [11-22].

## MATERIALS AND METHODS

### Materials

Cefprozil was gift sample from Natco labs, Hyderabad, India. Guargum, Chitosan, Sodium carboxy methyl cellulose, MCC $p^H$102 from SD Fine Chemicals Mumbai India. Magnesium stearate, Talc from Merck Specialities Pvt Ltd, Mumbai, India

### Drug – Excipient compatibility studies

### Fourier Transform Infrared (FTIR) spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a

Corresponding Author :- **Gollapudi Rajesh** Email:- rajeshgollapudi@yahoo.com

suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes.

**Formulation development of Tablets**

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 6.3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Cefprozil. Total weight of the tablet was considered as 750mg [23-30].

**Evaluation of post compression parameters for prepared Tablets**

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

**Weight variation test:**

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula [31-44].

% Deviation = (Individual weight – Average weight / Average weight) × 100

**Hardness:**

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

**Thickness**

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

**Friability**

It is measurement of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre weighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were reweighed; loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [(W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

**Determination of drug content:**

Tablets were tested for their drug content. Ten tablets were finely powdered and quantity of the powder equivalent to one tablet weight of Cefprozil were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve [45-60].

***In vitro* drug release studies**

900ml 0f 0.1N HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. Tablet was placed in the vessel and the vessel was covered and the apparatus was operated for 2 hours and then the medium 0.1 N HCl was removed and pH 6.8 phosphate buffer was added and process was continued for up to 12 hrs at 50 rpm. At definite time intervals 5 ml of the receptor fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed spectrophotometrically at 298 nm using UV-spectrophotometer [61-70].

**Application of Release Rate Kinetics to Dissolution Data:**

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

**RESULTS AND DISCUSSION**

**Quality Control Parameters For tablets**

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***In-Vitro* Drug Release Studies**

From the dissolution data it was evident that the formulations prepared with guar gum as polymer were unable to retard the drug release up to desired time period

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i.e., 12 hours.

Whereas the formulations prepared with karaya gum retarded the drug release in the concentration of 125 mg showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.10% in 12 hours with good retardation.

**Application of Release Rate Kinetics to Dissolution Data**

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model [71-80].

From the above graphs it was evident that the formulation F6 was followed Zero order release kinetics.

**Table 1. Formulation composition for tablets**

| Formulation No. | Cefprozil | Guar gum | Karaya gum | Locust bean gum | Mg. Stearate | Talc | MCC pH 102 |
|---|---|---|---|---|---|---|---|
| F1 | 500 | 62.5 | | | 7 | 7 | QS |
| F2 | 500 | 125 | | | 7 | 7 | QS |
| F3 | 500 | | 62.5 | | 7 | 7 | QS |
| F4 | 500 | | 125 | | 7 | 7 | QS |
| F5 | 500 | | | 62.5 | 7 | 7 | QS |
| F6 | 500 | | | 125 | 7 | 7 | QS |
| F7 | 500 | 62.5 | 62.5 | | 7 | 7 | QS |
| F8 | 500 | | 62.5 | 62.5 | 7 | 7 | QS |
| F9 | 500 | 62.5 | | 62.5 | 7 | 7 | QS |

All the quantities were in mg.

**Table 2. Post Compression Parameters of Tablets**

| Formulation codes | Weight variation(mg) | Hardness(kg/cm2) | Friability (%loss) | Thickness (mm) | Drug content (%) |
|---|---|---|---|---|---|
| F1 | 752.5 | 4.5 | 0.50 | 6.8 | 99.76 |
| F2 | 755.4 | 4.5 | 0.51 | 6.9 | 99.45 |
| F3 | 748.6 | 4.4 | 0.51 | 4.9 | 99.34 |
| F4 | 750.6 | 4.5 | 0.55 | 6.9 | 99.87 |
| F5 | 759.4 | 4.4 | 0.56 | 6.7 | 99.14 |
| F6 | 750.7 | 4.5 | 0.45 | 6.5 | 98.56 |
| F7 | 752.3 | 4.1 | 0.51 | 6.4 | 98.42 |
| F8 | 751.2 | 4.3 | 0.49 | 6.7 | 99.65 |
| F9 | 748.3 | 4.5 | 0.55 | 6.6 | 99.12 |

**Table 3. Dissolution Data of Cefprozil Tablets Prepared With Guar gum In Different Concentrations**

| Time (hr) | Cumulative Percent Drug Dissolved (n=3±SD) | | |
|---|---|---|---|
| | F1 | F2 | F3 |
| 0.5 | 25.5 | 20.1 | 16.4 |
| 1 | 46.7 | 39.4 | 26.7 |
| 2 | 76.5 | 55.3 | 34.6 |
| 3 | 98.4 | 75.3 | 42.4 |
| 4 | | 87.3 | 55.4 |
| 5 | | 99.4 | 67.4 |
| 6 | | | 85.4 |
| 7 | | | 91.5 |
| 8 | | | 97.3 |

**Table 4. Dissolution Data of Cefprozil Tablets Prepared with Karaya gum in Different Concentrations**

| Time (hr) | Cumulative Percent Drug Dissolved (n=3±SD) | | |
|---|---|---|---|
| | F4 | F5 | F6 |
| 0.5 | 17.25 | 16.42 | 14.62 |
| 1 | 38.26 | 25.73 | 19.86 |

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| | | | |
|---|---|---|---|
| 2 | 54.16 | 36.63 | 22.35 |
| 3 | 72.01 | 45.04 | 31.45 |
| 4 | 88.26 | 58.25 | 39.80 |
| 5 | 97.10 | 65.33 | 45.25 |
| 6 | | 76.41 | 58.24 |
| 7 | | 84.84 | 66.73 |
| 8 | | 97.80 | 71.34 |
| 9 | | | 75.52 |
| 10 | | | 82.17 |
| 11 | | | 87.10 |
| 12 | | | 96.10 |

**Table 5. Dissolution Data of Cefprozil Tablets Prepared With locust bean gum In Different Concentrations**

| Time (hr) | Cumulative Percent Drug Dissolved (n=3±SD) | | |
|---|---|---|---|
| | F7 | F8 | F9 |
| 0.5 | 10.4 | 9.4 | 8.5 |
| 1 | 16.5 | 15.6 | 14.5 |
| 2 | 28.6 | 21.4 | 18.4 |
| 3 | 39.5 | 36.7 | 23.4 |
| 4 | 48.5 | 42.4 | 28.2 |
| 5 | 59.4 | 49.6 | 34.8 |
| 6 | 69.2 | 55.3 | 40.2 |
| 7 | 74.5 | 60.3 | 44.8 |
| 8 | 82.3 | 72.8 | 50.4 |
| 9 | 87.78 | 83.52 | 63.34 |
| 10 | 98.78 | 88.65 | 69.27 |
| 11 | | 96.56 | 74.86 |
| 12 | | | 79.97 |

**Table 6: Release kinetics data for optimised formulation**

| Cumulative (%) Release Q | Time (T) | Log (%) Release | Log (%) Remain | Release Rate (Cumulative % Release / t) | 1/Cum% Release | Peppas log Q/100 | % Drug Remaining |
|---|---|---|---|---|---|---|---|
| 0 | 0 | | 2.000 | | | | 100 |
| 14.62 | 0.5 | 1.165 | 1.931 | 29.240 | 0.0684 | -0.835 | 85.38 |
| 19.86 | 1 | 1.298 | 1.904 | 19.860 | 0.0504 | -0.702 | 80.14 |
| 22.35 | 2 | 1.349 | 1.890 | 11.175 | 0.0447 | -0.651 | 77.65 |
| 31.45 | 3 | 1.498 | 1.836 | 10.483 | 0.0318 | -0.502 | 68.55 |
| 39.8 | 4 | 1.600 | 1.780 | 9.950 | 0.0251 | -0.400 | 60.2 |
| 45.25 | 5 | 1.656 | 1.738 | 9.050 | 0.0221 | -0.344 | 54.75 |
| 58.24 | 6 | 1.765 | 1.621 | 9.707 | 0.0172 | -0.235 | 41.76 |
| 66.73 | 7 | 1.824 | 1.522 | 9.533 | 0.0150 | -0.176 | 33.27 |
| 71.34 | 8 | 1.853 | 1.457 | 8.918 | 0.0140 | -0.147 | 28.66 |
| 75.52 | 9 | 1.878 | 1.389 | 8.391 | 0.0132 | -0.122 | 24.48 |
| 82.17 | 10 | 1.915 | 1.251 | 8.217 | 0.0122 | -0.085 | 17.83 |
| 87.1 | 11 | 1.940 | 1.111 | 7.918 | 0.0115 | -0.060 | 12.9 |
| 96.1 | 12 | 1.983 | 0.591 | 8.008 | 0.0104 | -0.017 | 3.9 |

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**Fig 1. FTIR graph of Pure drug**

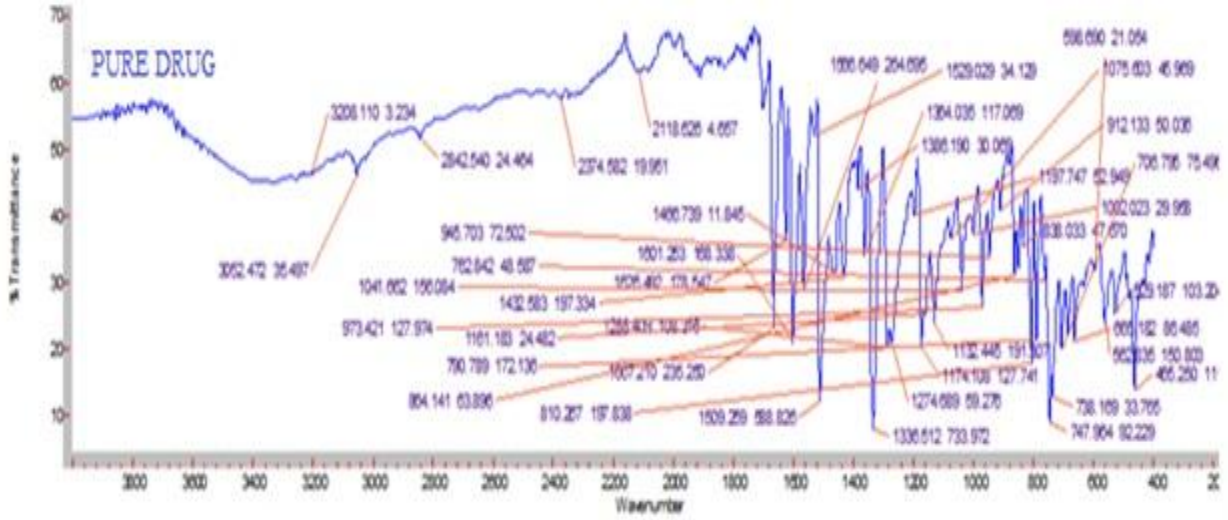


**Fig 2. FTIR graph of Optimised formulation**

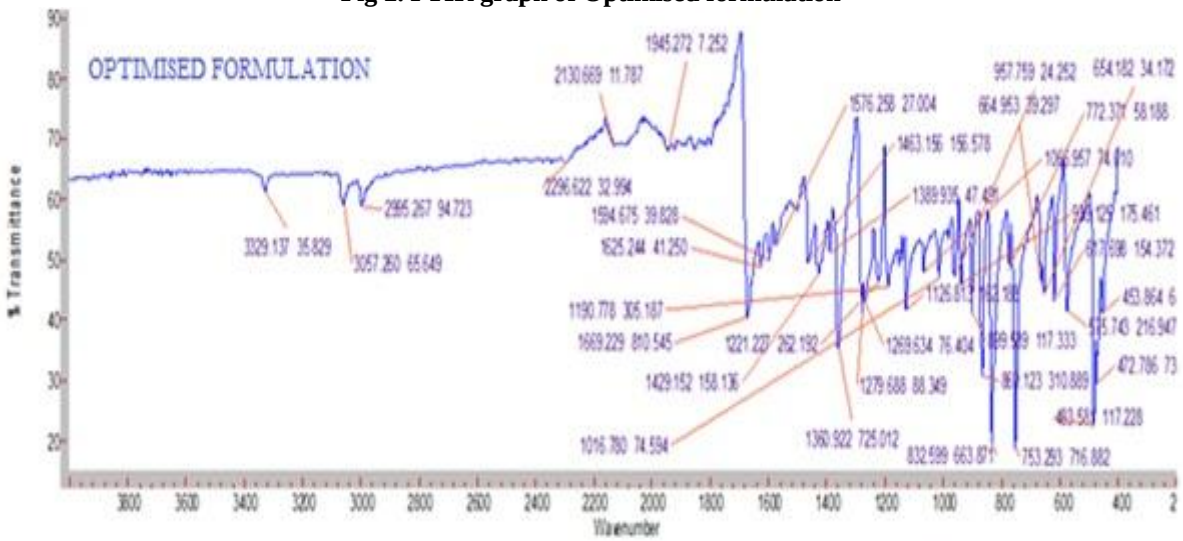


**Fig 3. Dissolution profile of Cefprozil (F1, F2, F3 formulations)**

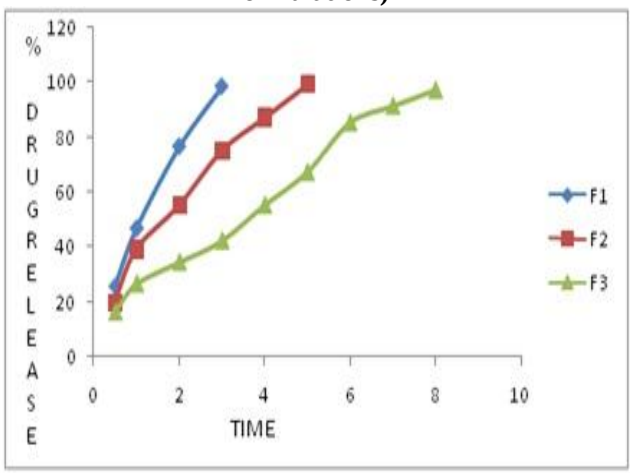


**Fig 4. Dissolution profile of Cefprozil (F4, F5, F6 formulations)**

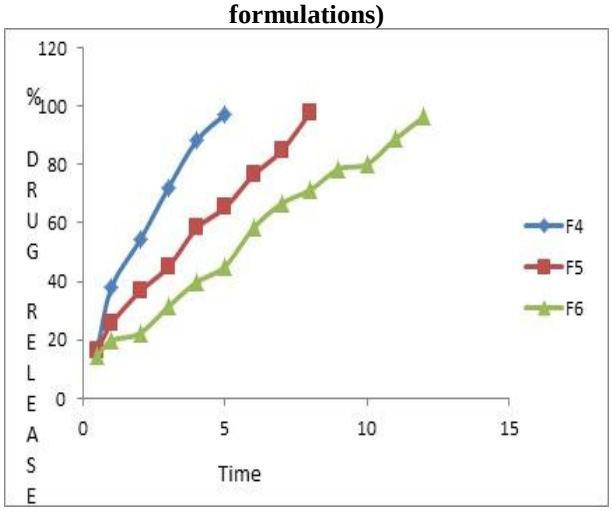

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**Fig 5. Dissolution profile of Cefprozil (F7, F8, F9 formulations)**

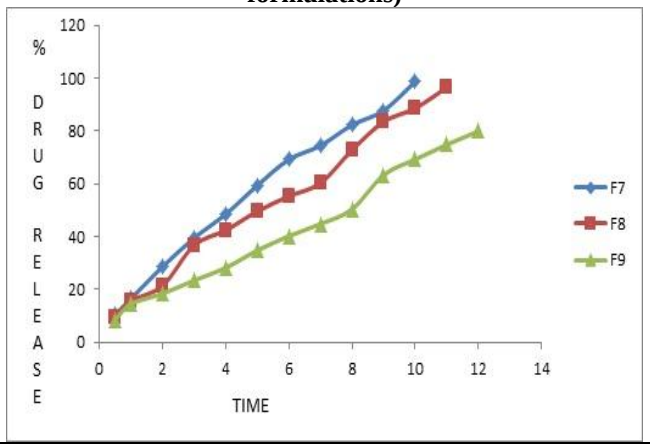



**Fig 6. Zero order release kinetics graph**

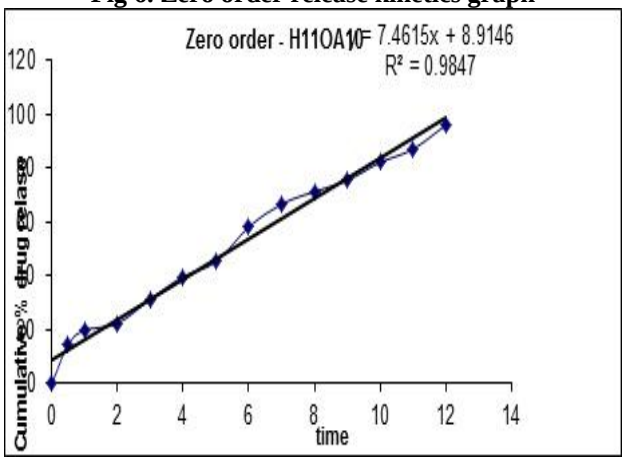



**Fig 7. Higuchi release kinetics graph**

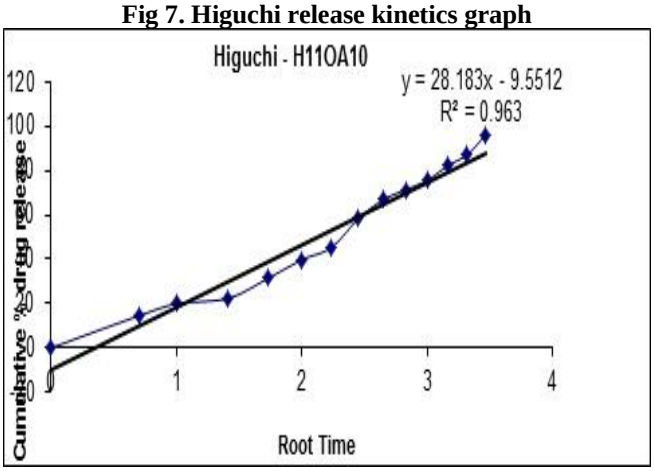



**Fig 8. Kars mayer peppas graph**

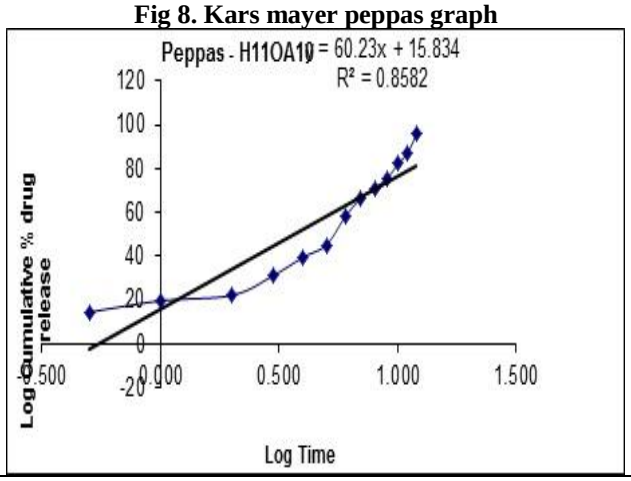
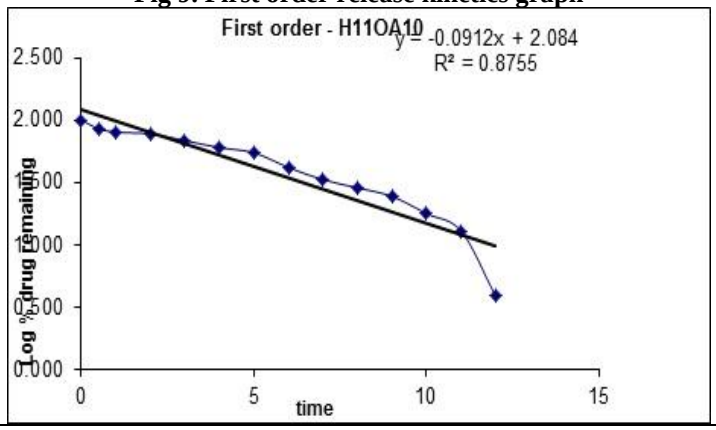



**Fig 9. First order release kinetics graph**




## CONCLUSION

The aim of the present study was to develop sustained release formulation of Cefprozil to maintain constant therapeutic levels of the drug for over 12 hrs. Various natural polymers such as Guar gum, karaya gum and locustbean gum were employed as polymers. Cefprozil dose was fixed as 500 mg. Total weight of the tablet was considered as 750 mg. Polymers were used in the concentration of 62.5 mg and 125 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

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