International Journal of Current Trends in Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijctpr

Research Article Open Access

# Formulation and *In-Vitro* Evaluation of Gastro Retention Floating Tablets of Cefuroxime Axetil

**Dr. R. Srinivasan, K. Vinod Kumar*, G. Lakshmana, D. Rajesh Kumar, P. Thrinadh**

*Siddhartha Institute of Pharmaceutical Sciences, Jonnalagadda, Narsaraopet, Guntur, Andhra Pradesh, India*

**A B S T R A C T**

In the present research work gastro retentive floating matrix formulation of Cefuroxime axetil by using various hydrophilic polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC as polymeric substances. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations guar gum as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 180 mg. whereas in low concentrations the polymer was unable to produce the desired action. (F12 Formulation, 98.52% Drug release). The formulations prepared with HPMC K100M were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed fickian peppas order mechanism of drug release.

**Keywords:** Cefuroxime axetil , HPMC polymers , Floating tablets

**A R T I C L E I N F O**

**CONTENTS**

1. Introduction . . . . . 759
2. Materials and Methods . . . . . 759
3. Results and discussion . . . . . 760
4. Conclusion . . . . . 762
5. References . . . . . 762

**Article History: Received** 27 September 2014, **Accepted** 15 November 2014, **Available Online** 15 January 2015

***Corresponding Author**
K. Vinod Kumar
Assistant professor
Siddhartha Institute of pharmaceutical sciences, Narsaraopet, Guntur, A.P, India
Manuscript ID: IJCTPR2401

PAPER-QR CODE

**Citation:** K. Vinod Kumar, et al. Formulation and *In-Vitro* Evaluation of Gastro Retention Floating Tablets of Cefuroxime Axetil. *Int. J. Curnt. Tren. Pharm, Res.*, 2015, 3(1): 758-762.

## 1. Introduction

Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro retentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs [1].

The floating drug delivery system (FDDS) also called Hydro dynamically Balanced Drug Delivery System (HBS). FDDS is an oral dosage forms (capsule or tablet) designed to prolong the residence time of the dosage form within the GIT. It is a formulation of a drug with gel forming hydrocolloids meant to remain buoyant on stomach contents [2,3].

**Advantages of FDDS:**

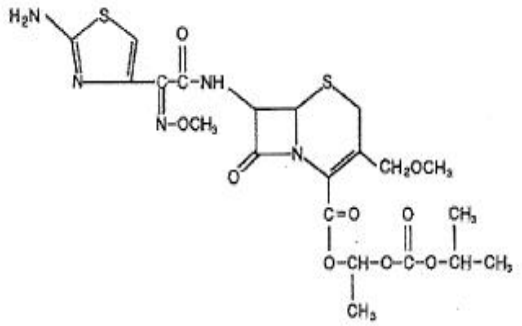
a. Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.
b. FDDS are advantageous for drugs meant for local action in the stomach e.g.: Antacids.
c. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
**d.** The FDDS are advantageous for drugs absorbed through the stomach e.g.: Ferrous salts, Antacids[4,5]

**Disadvantages of FDDS:**

a. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
b. Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.
**c.** Drugs that may irritate the stomach lining or are unstable in its acidic environment should not be formulated in gastro retentive systems [5,6].

**Drug Profile[7]:**

**Chemical structure:**



**Chemical Name:** (RS)1(isopropoxycarbonyloxy) ethyl (+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-{(Z)methoxy imino} acetamido]-3methoxymethyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene- 2-carboxylate.

**Molecular Formula:** $C_{21}H_{27}N_5O_9S_2$

**Molecular weight:** 557,6.

**Category:** semi-synthetic antibiotic of the cephalosporin class

## 2. Materials and Methods

**Preformulation parameters:**

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia, they were

A. Angle of repose
B. Bulk density
C. Tapped density
D. Measures of powder compressibility

**Formulation development of Tablets:** All the formulations were prepared by direct compression..The tablets were prepared as per the procedure given below and aim is to prolong the release of Cefuroxime axetil. Total weight of the tablet was considered as 650mg.

**Procedure:**

a. Cefuroxime axetil and all other ingredients were individually passed through sieve no ≠ 60.
b. All the ingredients were mixed thoroughly by triturating up to 15 min.
c. The powder mixture was lubricated with talc.
**d.** The tablets were prepared by using direct compression method.

**Optimization of Sodium bicarbonate concentration:**

**Table 1:** Optimization sodium bicarbonate concentration

| S.No | Excipient Name | EF1 | EF2 | EF3 |
|---|---|---|---|---|
| 1 | Cefuroxime axetil | 200 | 200 | 200 |
| 2 | HPMC K 100M | 200 | 200 | 200 |
| 4 | $NaHCO_3$ | 45 | 60 | 90 |
| 5 | Mg.Stearate | 6 | 6 | 6 |
| 5 | Talc | 6 | 6 | 6 |
| 7 | MCC pH 102 | Q.S | Q.S | Q.S |

All the quantities were in mg. Total weight is 600 mg.

Based on the floating lag time and floating duration the concentration of sodium bicarbonate was optimised.

**Table 2:** Formulation composition for floating tablets

| Formulation No. | Cefuroxime axetil | HPC | HPMC K100M | Guar gum | $NaHCO_3$ | Mag. Stearate | Talc | MCC pH 102 |
|---|---|---|---|---|---|---|---|---|
| F1 | 200 | 60 | | | 90 | 6 | 6 | QS |
| F2 | 200 | 90 | | | 90 | 6 | 6 | QS |
| F3 | 200 | 120 | | | 90 | 6 | 6 | QS |
| F4 | 200 | 180 | | | 90 | 6 | 6 | QS |
| F5 | 200 | | 60 | | 90 | 6 | 6 | QS |
| F6 | 200 | | 90 | | 90 | 6 | 6 | QS |
| F7 | 200 | | 120 | | 90 | 6 | 6 | QS |
| F8 | 200 | | 180 | | 90 | 6 | 6 | QS |
| F9 | 200 | | | 60 | 90 | 6 | 6 | QS |
| F10 | 200 | | | 90 | 90 | 6 | 6 | QS |
| F11 | 200 | | | 120 | 90 | 6 | 6 | QS |
| F12 | 200 | | | 180 | 90 | 6 | 6 | QS |

All the quantities were in mg

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

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

## 3. Results and Discussion

The present study was aimed to developing gastro retentive floating tablets of Cefuroxime axetil using various HPMC polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

**Analytical Method**: Graphs of Cefuroxime axetil was taken in Simulated Gastric fluid (pH 1.2) at 262nm.

**Table 3:** Observations for graph of Cefuroxime axetil in 0.1N HCl (298nm)

| Concertration[µg/l] | Absorbance |
|---|---|
| 0 | 0 |
| 5 | 0.207 |
| 10 | 0.341 |
| 15 | 0.458 |
| 20 | 0.582 |
| 25 | 0.682 |

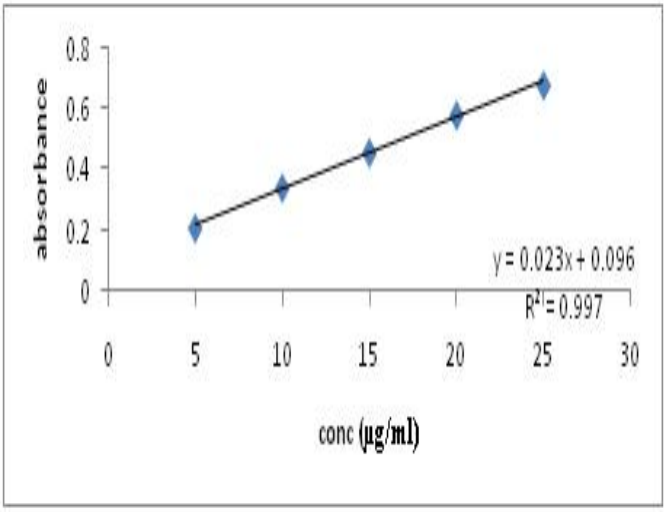



**Figure 1:** Standard graph of Cefuroxime axetil in 0.1N HCl

**Table.04.Preformulation parameters of powder blend**

| Formulation Code | Angle of Repose | Bulk density (gm/ml) | Tapped density (gm/ml) | Carr's index (%) | Hausner's Ratio |
|---|---|---|---|---|---|
| F1 | 27.91 | 0.45 | 0.55 | 18.18 | 1.22 |
| F2 | 28.23 | 0.47 | 0.55 | 14.54 | 1.17 |
| F3 | 29.34 | 0.50 | 0.58 | 13.79 | 1.16 |
| F4 | 26.71 | 0.46 | 0.55 | 16.36 | 1.19 |
| F5 | 29.34 | 0.50 | 0.58 | 13.79 | 1.16 |
| F6 | 28.23 | 0.47 | 0.55 | 14.54 | 1.17 |
| F7 | 29.34 | 0.50 | 0.58 | 13.79 | 1.16 |
| F8 | 26.78 | 0.41 | 0.50 | 18 | 1.21 |
| F9 | 26.78 | 0.41 | 0.50 | 18 | 1.21 |
| F10 | 29.34 | 0.50 | 0.58 | 13.79 | 1.16 |
| F11 | 26.78 | 0.41 | 0.50 | 18 | 1.21 |
| F12 | 26.78 | 0.41 | 0.50 | 18 | 1.21 |

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.41 to 0.50 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the

formulations was found to be in the range of 0.50 to 0.58 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 14 to 18 which show that the powder has good flow properties. All the formulations has shown the hausner's ratio ranging between 0 to 1.2 indicating the powder has good flow properties.

**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 tablets.

**Table 5:** Quality Control Parameters

| Formulation Codes | Weight variation(mg) | Hardness (kg/cm2) | Friability (%loss) | Thickness (mm) | Drug content (%) | Flaoting lag time (min) |
|---|---|---|---|---|---|---|
| F1 | 605.5 | 4.5 | 0.51 | 4.8 | 98.76 | 5.0 |
| F2 | 604.4 | 4.5 | 0.51 | 4.9 | 97.45 | 5.2 |
| F3 | 600..6 | 4.4 | 0.52 | 4.9 | 102.34 | 5.5 |
| F4 | 611.6 | 4.5 | 0.53 | 4.9 | 101.87 | 5.1 |
| F5 | 600.4 | 4.4 | 0.54 | 4.7 | 104.14 | 5.0 |
| F6 | 609.7 | 4.3 | 0.50 | 4.5 | 98.56 | 5.4 |
| F7 | 601.3 | 4.3 | 0.53 | 4.4 | 108.42 | 5.5 |
| F8 | 600.2 | 4.3 | 0.50 | 4.7 | 103.65 | 5.6 |
| F9 | 604.3 | 4.4 | 0.51 | 4.6 | 104.12 | 5.7 |
| F10 | 611.6 | 4.5 | 0.53 | 4.9 | 101.87 | 5.1 |
| F11 | 600.4 | 4.4 | 0.54 | 4.7 | 104.14 | 5.0 |
| F12 | 609.7 | 4.3 | 0.50 | 4.5 | 98.56 | 5.4 |

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

**Dissolution profile of Cefuroxime axetil floating tablets (F9, F10, F11,F12 formulations)**

From the dissolution data it was evident that the formulations prepared with HPC as polymer were unable to retarded the drug release up to desired time period i.e., 12 hours. Whereas the formulations prepared with HPMC K100M were retarded the drug release in more than 12 hours in higher concentrations. In lower concentrations the polymer was unable to retard the drug release. At 90 mg concentrations of HPMC K100M was showed maximum drug release up to 12 hours. (F6-97.37%). The formulations prepared with Guar gum showed very good retardation capacity hence they were considered. Finally F12 formulation containing guar gum in the concentrations of 180 mg. It showed drug release of 98.52 in 12 hours.

**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.

**Table 6:** Release kinetics data for optimised formulation (F12)

| Cumulative (%) release Q | Time ( T ) | Root ( T) | Log ( %) Release | Log ( T ) | Log (%) Remain | Release Rate (Cumulative % Release / t) | 1/CUM % Release | Peppas log Q/100 | % Drug Remaining |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | | | 2.000 | | | | 100 |
| 15.87 | 0.5 | 0.707 | 1.201 | 0.301 | 1.925 | 31.740 | 0.0630 | -0.799 | 84.13 |
| 20.19 | 1 | 1.000 | 1.305 | 0.000 | 1.902 | 20.190 | 0.0495 | -0.695 | 79.81 |
| 33.32 | 2 | 1.414 | 1.523 | 0.301 | 1.824 | 16.660 | 0.0300 | -0.477 | 66.68 |
| 37.13 | 3 | 1.732 | 1.570 | 0.477 | 1.798 | 12.377 | 0.0269 | -0.430 | 62.87 |
| 49.71 | 4 | 2.000 | 1.696 | 0.602 | 1.701 | 12.428 | 0.0201 | -0.304 | 50.29 |
| 55.97 | 5 | 2.236 | 1.748 | 0.699 | 1.644 | 11.194 | 0.0179 | -0.252 | 44.03 |
| 61.77 | 6 | 2.449 | 1.791 | 0.778 | 1.582 | 10.295 | 0.0162 | -0.209 | 38.23 |
| 66.32 | 7 | 2.646 | 1.822 | 0.845 | 1.527 | 9.474 | 0.0151 | -0.178 | 33.68 |
| 70.64 | 8 | 2.828 | 1.849 | 0.903 | 1.468 | 8.830 | 0.0142 | -0.151 | 29.36 |
| 79.24 | 9 | 3.000 | 1.899 | 0.954 | 1.317 | 8.804 | 0.0126 | -0.101 | 20.76 |
| 85.32 | 7 | 3.162 | 1.931 | 1.000 | 1.167 | 8.532 | 0.0117 | -0.069 | 14.68 |
| 90.73 | 8 | 3.317 | 1.958 | 1.041 | 0.967 | 8.248 | 0.0110 | -0.042 | 9.27 |
| 98.52 | 9 | 3.464 | 1.994 | 1.079 | 0.170 | 8.210 | 0.0102 | -0.006 | 1.48 |

## 4. Conclusion

In the present research work gastro retentive floating matrix formulation of Cefuroxime axetil by using various hydrophilic polymers were developed. Initially analytical method development was done for the drug molecule. Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent sodium bicarbonate concentration was optimized. Then the formulation was developed by using different concentrations of polymers of various grades of HPMC as polymeric substances. The formulation blend was subjected to various preformualation studies, flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. Among all the formulations the formulations guar gum as polymer were retarded the drug release up to desired time period i.e., 12 hours in the concentration of 180 mg. whereas in low concentrations the polymer was unable to produce the desired action. (F12 Formulation, 98.52% Drug release). The formulations prepared with HPMC K100M were also retarded the drug release for more than 12 hours. Hence they were not considered. The optimized formulation dissolution data was subjected to release kinetics, from the release kinetics data it was evident that the formulation followed fickian peppas order mechanism of drug release.

## 5. References


1. Leon Lachman, Herbert A. Liberman, the Theory and Practice of Industrial Pharmacy: pp.293-302.
2. Robinson Jr, Lee V.H.L, Controlled drug delivery: Fundamentals and Applications, 2nd edn. Marcel Dekker, New york: **1978**, pp.24-36.
3. Brahmankar D.M, Jaiswal S.B, Biopharmaceutics and Pharmacokinetics a treatise, 1st ed. Vallabh prakashan; New Delhi: **1995**, pp. 64-70.
4. H.G. Sivakumar, Floating Drug Delivery System for Prolonged Gastric Residence time: A review, Ind. J. Pharm. Edu., **2004**: pp. 311-316.
5. Chein Y.W, Novel Drug Delivery Systems, 2nd ed.: Marcel Dekker; New York: **1992**, pp.4-56.
6. Ansel, Pharmaceutical Dosage form and Drug Delivery System, Lipincott, 7th edition: pp. 553.
7. http://www.drugbank.ca/drugs/DB01233