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# DESIGN AND CHARACTERIZATION OF SUSTAINED RELEASE MINI-TABLETS OF CEFIXIME TRIHYDRATE

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# ABSTRACT

Sustained release (SR) dosage forms (mini tablets) are designed to a drug release in a predetermined rate by maintaining a constant drug level for a particular period of time with minimum side effects. Here investigation involves design and characterization of sustained release mini-tablets of cefixime trihydrate intended for prolong the drug release in the GIT and consequently into the blood. The SR mini tablets were prepared by using different polymers, which are gaur gum, xantan gum, HPMCK<sub>15</sub>, Eudragit RL<sub>100</sub>. The tablets were prepared by wet granulation method; among the twelve one formulationF8, F11 shows acceptable good results. In-vitro dissolution studies were performed to 12hrs in pH 6.8 phosphate buffer Formulation F8, F11 exhibits 98.2%. 98.8% of drug within 12hrs respectively all formulations were carried out for model fitting analysis by treating the data according to zero order kinetics and korsmayer-peppas equation. F8, F11 Followed zero order kinetics, stability studies were performed for formulation F8, F11 at 25°c/60%RH and 40°c/75RH for 30days. The results of stability studies exhibit no change in physical appearance of drug.

# **KEY WORDS**

Sustained release, Mini-tablets, polymers (Gurgum, HPMCK15, Xantan gum, Eudragit RL100

# **1. INTRODUCTION**

Despite grate advancement in drug delivery, oral route is preferred route for the administration of therapeutic agent, low cost of therapy, ease of administration and cause to higher levels of patient compliance. 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. Conventional dosage forms such as tablets, capsules provide specific drug concentration in blood without offering any control over drug delivery and also cause grate fluctuations in plasma drug levels. Various approaches have been carried out to improve the drug release over an extend period of time with administration of oral single dose and without showing any fluctuations in plasma drug concentration. Introduction of Mini-tablet as Sustained release (SR) has given a new breakthrough for novel drug delivery system (NDDS) in the field of Pharmaceutical technology.

Active drug substance selected for the project: Cefixime trihydrate

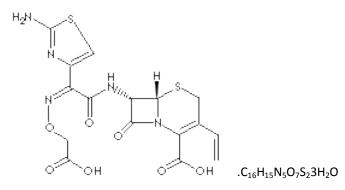
Category of the drug:3<sup>rd</sup> generation Cephalosporin antibiotic

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Mini-tabs are smaller tablets with a diameter typically equal to or less than 3 mm that are filled into a capsule, or occasionally, can be compressed into larger tablets. These combinations may include immediate release, sustain release, and/or control release It is also possible to incorporate mini-tabs of different drugs to treat concurrent diseases or combinations of drugs to improve overall therapeutic outcome.

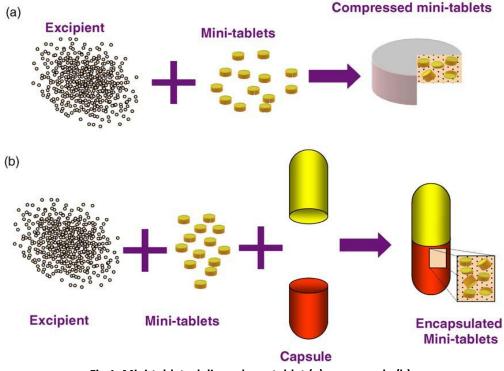


Fig.1. Mini-tablets delivered as a tablet (a) or a capsule (b).

**2. SUSTAINED- RELEASE DOSAGE FORMS**: <sup>2, 3, and 6</sup> It is defined as "any drug or dosage form modification that prolongs the therapeutic activity of the drug". It provides prolonged but not necessarily uniform release of drug. The United States Pharmacopoeia has

adopted the term extended release whereas the

British Pharmacopoeia has adopted the term slow release. United States Food and Drug Administration has adopted the term Prolonged release. However the literature survey indicates that the most widely used terms today are sustained release & controlled release.

 $P_{age}80$ 

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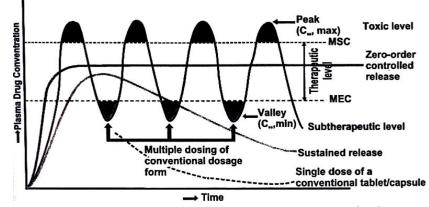


Figure 2: A hypothetical plasma concentration – time profile from conventional multiple and single doses of sustained and controlled delivery formulations

# **2.1.** Potential advantages of sustained release systems:

- Avoid patient's compliance problems.
- Employ less total drug.
- Minimize or eliminate local side effects.
- Minimize or eliminate systemic side effects.
- Obtain less potentiation or reduction in drug activity with chronic use.
- Minimize drug accumulation with chronic dosing.
- Improve efficiency in treatment.
- Cures or controls condition more promptly.
- Improves control of condition i.e., reduced fluctuation in drug level.
- Improves bioavailability of some drugs.
- Make use of special effects, e.g. sustainedrelease aspirin for morning relief of arthritis by dosing before bed time.

Economy i.e. reduction in health care costs. The average cost of treatment over an extended time period may be less, with less frequency of dosing, enhanced therapeutic benefits and reduced side effects. The time required for health care personnel to dispense and administer the drug and monitor patient is also reduced.

# **3. MATERIAL AND METHODS**

# 3.1. Materials

Cefixime trihydrate [API] Reddy labs; Hyderabad; hydroxyl propyl methyl cellulose (HPMC K-15) From Neha chemicals Hyderabad S; Methanol, S.D. Fine chemicals, Mumbai; Xantan gum Neha chemicals, Hyderabad; Gurgum, Neha chemicals, Hyderabad; Ethyl cellulose, Neha chemicals, Hyderabad; Sodium hydroxide From loba Chemie pvt. Ltd, Mumbai; Potassium di-hydrogen orthophosphate received from sigma-Aldrich Ltd, Delhi; Micro crystalline cellulose Neha chemicals, Hyderabad; Talc, prime laboratoires; Hyderabad.

# **3.2.** Formulation and Preparation of sustained release mini-tablets:

Sustained release mini-tablets were prepared by wet granulation method. The tablets were prepared by wet granulation technique. Weighed amounts of Cefixime trihydrate (API), Polymers (HPMC K<sub>15</sub>, Guar gum, Xantan gum, Eudragit RL<sub>100</sub> and Micro crystalline cellulose (diluents), were taken into a motor pestle by passing through a 40 mesh screen and mixed manually for 5 min. Then the blend was granulated with PVPK-30 using ethanol as the granulating agent. The mass was dried in a hot air oven at 50°C and sieved through a 30 mesh screen. Talc (glidant), Magnesium stearate (Lubricant) were then added to the dried, sieved Granules and mixed for about 5 min in a poly-bag. The produced mixture was compressed into tablets using a mini punching machine equipped with a 6 mm biconcave-faced punch.

#### **4. EVALUATION**

# 4.1. Pre-compression parameters:

#### 4.1.1. Angle of repose

Static angle of repose was measured according to the fixed funnel and free standing core method of Banker and Anderson. Blends were carefully poured through

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the Enar reposograph until the apex of the conical pile so formed just reached the tip of the funnel of reposograph. Height of instrument was fixed to 4 cm. Thus, with r being the radius of the base of the granules conical pile and the angle of repose ( $\theta$ ) was calculated by using the eqn. 1

#### $\tan \theta = h/r$ ,

#### Therefore, $\theta$ = tan-1 h/r... (1)

#### 4.1.2. Bulk density/Tapped density

Both bulk density (BD) and tapped density (TD) were determined. A suitable amount of powder blend from each formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 100 mL measuring cylinder. After observing its initial volume, the cylinder in the density tapper instrument and density is measured according to USP method II (up to1250 taps). The tapping was continued until no further change in volume was noted. Volume of packing after tapping was noted. BD and TD were calculated using eqn. 2 and 3 respectively.

BD = weight of the powder / volume of the packing... (2)

TD = weight of the powder / tapped volume of the packing... (3)

#### 4.1.3. Compressibility index

Compressibility index of the powder was determined by Carr's compressibility index [10] as given by equation 4

#### Carr's index (%) = [(TD – BD) x 100] / TD... (4)

It helps in measuring the force required to break the Friction between the particles and the hopper

#### 4.1.4 Determination of Melting Point

Melting point of cefixime tri hydrate was determined by capillary method. Fine powder of cefixime tri hydrate was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermo meter and the thermometer was placed in fire. The powder at what temperature it will melt was noticed.

#### 4.1.5. Hausner's ratio

It is the ratio of tapped to bulk density [11] and was calculated by using the eqn. 5

Hausner's ratio = TD/BD ... (5)

#### 4.2. Post-compression parameters:

The prepared tablets of Cefixime trihydrate were evaluated for quality control tests like hardness, Friability, weight variation, thickness, diameter, swelling index, floating or buoyancy test, drug Content uniformity and *in vitro* dissolution studies.

#### 4.2.1. Tablet hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and Handling, before usage, depends on its hardness.

The crushing strength of prepared tablets was determined for ten tablets of each batch using Monsanto hardness tester.

#### 4.2.2. 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 plastic chamber that revolves at 25 rpm for 4 minutes 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.

# % loss = Initial wt. of tablets - Final wt. of tablets/Initial wt. of tablets x 100... (6)

#### 4.2.3. Drug content

Drug content was determined by accurately weighing 5 tablets and crushing them in mortar with the help of a pestle. Then an accurately weighed quantity of powder equivalent to 5mg of drug was transferred to a 100 ml volumetric flask. 50 ml of methanol was added and shaken. Volume was made up to 100 ml with methanol. The solution was filtered through whatman filter paper. First few ml of the filtrate was discarded. 10 ml of the filtrate was diluted to 100 ml with methanol. From the above solution 1ml was taken and diluted to 10 ml with methanol. To the sample I mI of ninhydrin reagent was added and the mixture was heated in a water bath at 80 ± 5°C for 15 min. The flasks were cooled and then the amount of drug dissolved was determined bv UV spectrophotometer at 237nm against the reagent as blank. The drug content was calculated using following formula.

#### % Purity = 10 C (Au / As)

Where, C = concentration, Au and as are absorbance obtained from standard preparation and assay preparation respectively.

#### 4.2.4. Weight variation

Twenty tablets were weighed individually and the average weight was determined. Then percentage deviation from the average weight was calculated.

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According to USP standards, not more than the percentage shown in the table 2 and none deviates by more than twice that percentage.

#### 4.2.4. Tablet Thickness/ Diameter

Thickness and diameter of tablets was important for uniformity of tablet size. Six tablets were examined for their thickness and diameter using vernier calipers and the mean thickness and diameter value was calculated.

#### 4.2.5. Drug content uniformity:

Twenty mini-tablets weighted and crushed in a mortar. The fine powder, equivalent to 5mg of cefixime trihydrate was weighed and transferred into a 25ml calibrated volumetric flask and dissolved using,7.4pH Phosphate buffer to give a concentration of 1000µg/ml. Take 0.1 ml of this solution and diluted it upto10ml with 7.4pH Phosphate buffer solution to give a concentration of 10µg/ml. Absorbance measured 237nm using UV-Visible at spectrophotometer. Content uniformity was calculated using formula.

#### % Purity = 10 C (Au / As)

Where, C = concentration, Au and as are absorbance obtained from standard preparation and assay preparation respectively

#### 4.2.6. In vitro Dissolution studies

In-vitro dissolution study was performed by using USP Type II Apparatus (Paddle type) at 50rpm.0.1N Hcl (about 2hrs30min) and pH 7.4 phosphate buffer (about 12hrs); 900ml was used as dissolution medium which maintained at 37±0.5°C. 10ml dissolution medium was withdrawn at specific time intervals and replaced with same volume to maintain sink condition. Blank is pH 6.8 buffer in the case of dissolution media is buffer if dissolution media is 0.1N Hcl the blank is 0.1NHcl. After note the absorbance of samples by UV spectrophotometer at 237nm the concentration was calculated using standard calibration curve.

#### 4.2.7. Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product

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degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted. The International Conference on Harmonization (ICH) Guidelines titled "Stability testing of New Drug Substances and Products" describes the stability test requirements for drug registration application in the European Union, Japan and the States of America.

ICH specifies the length of study and storage conditions

Long-Term Testing: 25°C  $\pm$  2°C / 60% RH  $\pm$  5% for 12 Months

Accelerated Testing: 40°C  $\pm$  2°C / 75% RH  $\pm$  5% for 6 Months

#### 4.3. Drug release kinetics:

To study the release kinetics, data obtained from in vitro drug release studies were plotted in various kinetic models: zero order (Equation 1) as cumulative amount of drug released vs. time, first order (Equation 2) as log cumulative percentage of drug remaining vs. time, and Higuchi model (Equation 3) as cumulative percentage of drug released vs. square root of time.

#### C =K0 t ..... [Eqa1]

Where  $K_0$  is the zero-order rate constant expressed in units of concentration/time and t is the time in hours. A graph of concentration vs. time would yield a straight line with a slope equal to KO and intercept the origin of the axes.

LogC=LogC<sub>0</sub>-kt.2.303...... [Equ2]

Where  $C_0$  is the initial concentration of drug, k is the first order constant, and t is the time.

#### Q= Kt1/2..... [Equ3]

Where K is the constant reflecting the design variables of the system and t is the time in hours. Hence drug release rate is proportional to the reciprocal of the square root of time.[9] To evaluate the drug release with changes in the surface area and the diameter of the particles/tablets, the data were also plotted using the Hixson-Crowell cube root law

#### 3vQ<sub>0</sub>- 3vQt=KHC t...... [Equ4]

Where Qt is the amount of drug released in time t,  $Q_0$  is the initial amount of the drug in the tablet and KHC is the rate constant for the Hixson-Crowell rate equation as the cube root of the percentage of drug remaining in the matrix vs. time.

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# **5. RESULTS AND DISCUSSION**

The objective of the present work was design and characterization of cefixime trihydrate mini-tablets in sustained release dosage form by incorporating polymer matrix (HPMC k15, xanthan gum, gurgum, Eudragit RL100) which will prolong the drug release leading to minimize the peak and valley effect in the plasma and provide patient convenience.

The compatibility of the polymers and excipients was determined by IR spectroscopy and DSC results showed that the drugs are compatible with polymers and all excipients.

The granules were subjected to pre compression evaluation such as angle of repose, loose bulk density, tapped bulk density and compressibility index. It was concluded that granules exhibited good compressibility and flow property. three formulations containing HPMC k15 (1:0.5,1:0.75,1:1), other three formulations containing xanthangum (1:0.5,1:0.75,1:1) and also another three formulations have guargum polymer (1:0.5,1:0.75,1:1) and similarly three formulations containing Eudragit RL 100(1:0.5,1:0.75,1:1) were prepared.

It was concluded after the in-vitro dissolution study that formulation F8 (drug and gurgum ratio is 1:0.75) shows the best release profile also formulation F11 (drug and Eudragit RL100 polymer ratio is 1:0.75) shows good release profile in the group of such polymer combinations.

All the formulations were subjected to model fitting analysis by treating the data according to zero-order and korsmayer-peppas equations. F5, F6 followed higuchi and F1, F2, F4, F7, F8, F10, F11 followed zeroorder kinetics. Formulation F3, F9, F12 followed the first order kinetics.

Stability studies were conducted for F8 and F11 at 25°c/60 °c RH and 40 °c/75%RH for 30 days. The results of stability studies released no change in physical appearance, hardness, drug content and invitro dissolution profiles, thus indicating that formulations are stable.

| INGREDIENTS(mg/tab)         | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  | F9  | F10 | F11 | F12 |
|-----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| CEFIXIMETRIHYDRATE<br>(API) | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 00  | 200 |
| GUARGUM                     | 100 | 175 | 200 |     |     |     |     |     |     |     |     |     |
| XANTAN GUM                  |     |     |     | 100 | 175 | 200 |     |     |     |     |     |     |
| HPMCK15                     |     |     |     |     |     |     | 100 | 175 | 200 |     |     |     |
|                             |     |     |     |     |     |     |     |     |     | 100 | 175 | 200 |
| МСС                         | 110 | 35  | 10  | 110 | 35  | 10  | 110 | 35  | 10  | 110 | 35  | 10  |
| TALC                        | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   | 6   |
| MEGNESIUM<br>STEARATE       | 4   | 4   | 4   | 4   | 4   | 4   | 4   | 4   | 4   | 4   | 4   | 4   |
| TOTAL                       | 420 | 420 | 420 | 420 | 420 | 420 | 420 | 420 | 420 | 420 | 420 | 420 |

| Table.1: Composition | of mini-tablet | formulation (mg) |
|----------------------|----------------|------------------|
|----------------------|----------------|------------------|

Each mini tablet weight is 70mg, 6 mini tablets are filled in one capsule

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| Formulation | Angle of               | Loose Bulk                   | Tapped                      | Compressibity | Hasner's |
|-------------|------------------------|------------------------------|-----------------------------|---------------|----------|
| code        | repose( <sup>0</sup> ) | density (g/cm <sup>3</sup> ) | density(g/cm <sup>3</sup> ) | index (%)     | ratio    |
|             |                        |                              |                             |               |          |
| F1          | 32.1 <sup>0</sup>      | 0.250±0.003                  | 0.316±0.002                 | 9.25±0.02     | 1.26     |
| F2          | 33.0 <sup>0</sup>      | 0.255±0.001                  | 0.305±0.002                 | 7.53±0.03     | 1.19     |
| F3          | 31.4 <sup>0</sup>      | 0.306±0.002                  | 0.350±0.001                 | 6.12±0.04     | 1.14     |
| F4          | 4.3 <sup>0</sup>       | 0.274±0.002                  | 0.289±0.001                 | 8.16±0.04     | 1.05     |
| F5          | 31.5 <sup>0</sup>      | 0.356±0.001                  | 0.341±0.002                 | 9.2±0.01      | 0.95     |
| F6          | 32.0 <sup>0</sup>      | 0.284±0.002                  | 0.314±0.002                 | 6.5±0.01      | 1.10     |
| F7          | 32.7 <sup>0</sup>      | 0.376±0.001                  | 0.395±0.001                 | 5.9±0.02      | 1.050    |
| F8          | 33.6 <sup>0</sup>      | 0.304±0.001                  | 0.318±0.002                 | 10±0.03       | 1.04     |
| F9          | 34.0 <sup>0</sup>      | 0.411±0.002                  | 0.420±0.002                 | 6.54±0.02     | 1.021    |
| F10         | 31.1 <sup>0</sup>      | 0.274±0.001                  | 0.294±0.001                 | 6.95±0.04     | 1.07     |
| F11         | 33.7 <sup>0</sup>      | 0.309±0.002                  | 0.331±0.002                 | 7.64±0.03     | 1.07     |
| F12         | 32.6 <sup>0</sup>      | 0.264±0.001                  | 0.286±0.02                  | 8.5±0.02      | 1.08     |

#### Table.2: Pre-compression evaluation

#### **Table 3:Post-compression parameters**

| Formulation<br>code | Thickness<br>(mm)<br>Mean±<br>S.D(n=10) | Diameter<br>(mm)<br>Mean±<br>S.D(n=10) | Hardness<br>(kg/cm <sup>2)</sup><br>Mean±<br>S.D(n=10) | Weight<br>variation<br>Mean±S.D<br>(n=10) | Friability<br>(n=10)<br>(%) |
|---------------------|---|--|--|---|-----------------------------|
| F1                  | 3.98±0.083                              | 3±0.02                                 | 5.11±0.04  | 70±2%                                     | 0.45                        |
| F2                  | 3.02±0.04                               | 3±0.01                                 | 4.82±0.05  | 71±2%                                     | 0.41                        |
| F3                  | 3.1±0.070                               | 3 <b>±</b> 0.04                        | 5.32±0.03  | 72±2%                                     | 0.52                        |
| F4                  | 3.06±0.089                              | 3±0.03                                 | 5.70±0.05  | 73±2%                                     | 0.45                        |
| F5                  | 3.95±0.091                              | 3±0.02                                 | 4.88±0.03  | 69±2%                                     | 0.50                        |
| F6                  | 3.7±0.079                               | 3±0.02                                 | 4.26±0.10  | 68±2%                                     | 0.56                        |
| F7                  | 3.98±0.043                              | 3±0.01                                 | 3.95±0.05  | 70±2%                                     | 0.54                        |
| F8                  | 3.8±0.080                               | 3±0.04                                 | 6.08±0.05  | 71±2%                                     | 0.60                        |
| F9                  | 3.85±0.081                              | 3±0.04                                 | 5.02±0.03  | 72±2%                                     | 0.38                        |
| F10                 | 3.23±0.048                              | 3±0.03                                 | 5.41±0.04  | 69±2%                                     | 0.43                        |
| F11                 | 3.14±0.073                              | 3±0.02                                 | 5.98±0.05  | 72±2%                                     | 0.52                        |
| F12                 | 3.35±0.035                              | 3±0.04                                 | 5-6±0.05   | 69±2%                                     | 0.48                        |

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| TIME  | F1   | F2   | F3   | F4   | F5   | F6   | F7    | F8   | F9   | F10  | F11  | F12  |
|-------|------|------|------|------|------|------|-------|------|------|------|------|------|
| (hrs) |      |      |      |      |      |      |       |      |      |      |      |      |
| 1     | 19.8 | 17   | 14.4 | 21.6 | 19.3 | 23.4 | 19    | 19   | 7.2  | 18   | 12.6 | 18   |
| 2     | 27.9 | 25   | 17   | 25.6 | 23.4 | 27.4 | 21.6  | 27   | 18   | 27   | 21   | 25.6 |
| 3     | 37.3 | 32   | 29.7 | 36   | 31.5 | 29   | 30.1  | 39.5 | 24.7 | 37.8 | 22   | 30.6 |
| 4     | 48   | 40.5 | 42.7 | 47.2 | 44.5 | 38.7 | 39.2  | 43   | 31.5 | 48.2 | 29   | 43.2 |
| 5     | 55.8 | 43.2 | 50.4 | 64   | 55.3 | 43.6 | 47    | 50   | 37.8 | 55.1 | 37.8 | 49.5 |
| 6     | 63.9 | 54   | 63   | 85.5 | 68.8 | 49.5 | 58.2  | 60.2 | 45   | 63   | 49.5 | 53   |
| 7     | 67   | 56   | 67   | 95.4 | 82   | 55   | 65.5  | 65   | 51.3 | 70.4 | 55.8 | 57   |
| 8     | 71.5 | 63   | 69   | 96.3 | 85.5 | 59.8 | 72.4  | 71.5 | 54   | 81   | 63   | 63.1 |
| 9     | 73.8 | 64.8 | 75   | 100  | 91.8 | 63   | 84.6  | 77   | 61   | 90.2 | 67   | 67.6 |
| 10    | 81   | 72   | 80.5 | 105  | 96.7 | 69   | 95    | 83.5 | 66   | 98.8 | 75   | 71.8 |
| 11    | 88   | 76.5 | 85   | 109  | 101  | 74   | 104.2 | 91   | 73   | 109  | 88   | 76   |
| 12    | 93   | 82.8 | 87.3 | 112  | 109  | 82.8 | 110   | 98.5 | 75   | 117  | 98.8 | 79   |

Table 4: In vitro drug release data of Cefixime tri hydrate Sustained release minitablets:



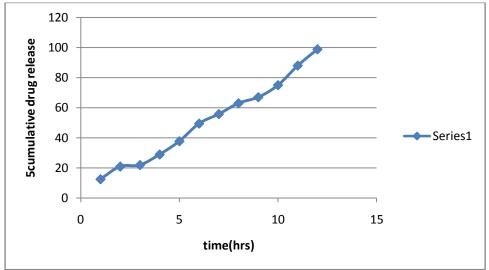


Table 5:Drug release kinetics of optimized formulation

| Formulation<br>code | Zero order | First order | Higuchi | Korsmeyer&<br>Peppas |
|---------------------|------------|-------------|---------|----------------------|
| F11                 | 0.984      | 0.962       | 0.909   | 0.955 & 0.775        |

Optimized formula F11 was selected to study different drug release kinetics to estimate the release mechanism. The straight line of linear regression analysis indicates zero order of the data yields the equation of best line with  $R^2$  value 0.984 and the slope of line corresponds to the zero order rate

constant was 7.671. The linearity was found in Higuchi equation plot ( $R^2$ =0.909) indicating the release of drug from dosage form as a square root of time dependent process based on Fickian diffusion. First order found to be 0.962. According to Korsmeyer

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where n is the release exponent, indicative of mechanism of drug release.

### CONCLUSION

The objective of study was to design and characterization of cefixime trihydrate sustained release mini-tablets found with retardant polymers. Which are prolonging the drug release causes to minimize the peak and valley effect in the plasma and provide good patient compliance. The compatibility studies, pre-compression evaluations, postcompression evaluations are shows acceptable results. F11 formulation was concluded as optimized formula based on the drug release profile; it was developed by using Eudragit RL100 (0.75%) as a rate retarding Polymers. Finally, the identified formula shall be utilized for the process development studies for successful launching of the product as it was proved to be stable and robust, cost effective compared to marketed tablet of Cefixime trihydrate (suprax). It can be easily conclude that SR formulations are aid in hike the efficiency of the dose additionally and more helpful in the case of Antibiotics in which irrationality of same May result in resistance.

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