*Research Article*

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# Formulation and evaluation of sustained released matrix tablets of losartn potassium

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## ABSTARCT

The basic goal of therapy is achieve a steady state blood or tissue levels that is therapeutically effective and non-toxic for an extended period of time. Sustained release drug delivery systems with aim the study of improved patient compliance, better therapeutic efficacy, less side effects and reduced dosage regimen with less toxicity for treatment for many acute and chronic diseases.Anti hypertensive drugs are used in the treatment of hypertension. Losartan potassium has been demonstrated to be superior to previous peptide receptor antagonists and angiotensin converting enzyme (ACE) inhibitors because of its enhanced specificity, selectivity and tolerability. Matrix tablets are very useful in the field of healthcare for sustained release dosage regimen. Keeping this in view, the present investigation has been aimed at designing suitable sustained release matrix tablets using polymers like HPMC K100M, Ethyl cellulose, Xanthan Gum by wet granulation method.

**Keywords:** Losartan potassium, HPMC K100M, Ethyl cellulose, Xanthan Gum, Wet granulation method.

## INTRODUCTION

### Oral Drug Delivery System

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drug via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as,

- Drugs with short half-life requires frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
- A typical peak- valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
- The unavoidable fluctuation in the drug concentration may lead to under medication or over medication as the cells, valves fall or rise beyond the therapeutic range.
- The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever over medication occurs.

It is a reasonable assumption that drug concentration at the site of action is related to drug plasma level and that, in the great majority of cases, the intensity of effect is some function of drug concentration at the target site. The objective of the most therapeutic regimens is to rapidly raise the plasma concentration to the required level and then to hold it constant for the desired duration of treatment .The extent to which this situation can be achieved depends on many factors, including the minimum effective concentration of the drug, the level at which side effects occur, the dose administered, the rate of drug release from the dosage form, the rate of elimination and the frequency of dosing. If the dose size and frequency of

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administration are correct, therapeutic 'steady state' levels of the drug can be achieved rapidly and maintained by the repetitive administration of conventional oral dosage forms.

- Inconvenience and/or difficult use of drugs with very short duration of action or biological half-life, thus needs frequent dosing.
- Traditionally, patient is expected to take medication during the daytime hours. Hence, plasma levels are likely to fall to sub–therapeutic levels overnight. Moreover the following major deficiencies of conventional dosage forms can reduce the patient's compliance to dose regimen.
- Potential for "peak-valley" plasma levels, leading to toxicity and side effects and incomplete therapy.
- Instances of adverse effects, forgetfulness, and inconvenience of dosage forms.
- Need for large systemic concentrations in order to achieve adequate concentration at target site or action.
- Potential variations in oral absorption due to variations in GIT pH profile, presence and type of food and transit time in gut.
- These above mentioned major deficiencies of drug therapy based on repetitive administration of conventional single oral dosage form, In order to overcome the drawbacks of conventional drug delivery system, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.

Thus, various modified drug products have been developed to release the active drug from the product at a controlled rate. The term controlled release drug products was previously used to describe various types of oral extended-release dosage forms, including sustained release, sustained action, prolonged action, slow release, long action, and retarded release.

## MATERIALS AND METHODS

### Evaluation of sustained release matrix tablets

### Appearance

The tablets were visually observed for capping, chipping, lamination and colour.

### Physicochemical characteristic

### Dimension (Thickness and Diameter)

The thickness and diameter of tablets were important for uniformity of tablet size. The thickness and diameter of the tablets was determined using a Vernier caliper.

### Tablet Hardness

The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm$^2$. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm$^2$.

### Friability

Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre weighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable. Percent friability(% F) was calculated as follows,

% F = (Initial Wt. - Final Wt. / Initial Wt.) x 100

### Drug content of losartan potassium

Content uniformity was determined by accurately weighing 20 tablets and crushing them in mortar. Then an accurately weighed quantity of powder equivalent to 20 mg of drug was transferred to a 100 ml volumetric flask. Few ml of water was added and shaken for 15 min. Volume was made up to 100 ml with distilled water. The solution was filtered through Whatmann filter paper and then 5 ml of the filtrate was diluted to 100 ml with 0.1N hydrochloric acid. Then absorbance of the resulting 10 □g/ml solution was recorded at 205.5 nm. Content uniformity was calculated using formula –

$$\% \text{ Purity} = 10\ C\ (Au / As) \quad \text{---------- (9)}$$

Where
C- Concentration,
Au and As - Absorbance's obtained from standard preparation and assay preparation respectively.

### Weight Variation

To find out weight variation 20 tablets of each formulation were weighed individually using an electronic balance and average was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

**Table 1: Specifications of % Weight Variation Allowed in Tablets as per Indian Pharmacopoeia.**

| Average weight of tablets (mg) | Maximum percent difference allowed |
|---|---|
| 80 or less | 10 |
| More than80 but less than 250 | 7.5 |
| 250 or more | 5 |

## *In-Vitro* Dissolution Studies

The in vitro dissolution was carried out by using USP type II dissolution apparatus was determined using USP Dissolution testing apparatus type-II (Paddle method; Veego Scientific VDA-8DR, Mumbai, India).

### Dissolution medium

0.1N hydrochloric acid for first 2 hours. pH 6.8 phosphate buffer for next 8 hours.

### Dose size

50mg.

### Average weight of tablet

250mg.

### Volume of medium

900ml.

### Speed of paddle

50 rpm.

### Temperature of dissolution medium

37± $1^0$ C.

The tablets were placed in the dissolution medium and the apparatus was run. At intervals of 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours 5 ml aliquots were withdrawn and replacement was done each time with equal amounts of fresh dissolution medium maintained at same temperature. Each 5 ml aliquot was filtered through Whatman filter paper (No.41). 5 ml of sample was diluted to 10 ml 0.1N Hydrochloric acid for first 2 hours and then with pH 6.8 phosphate buffer for next 8 hours and absorbance of these solutions was measured at 205.5 nm using a Shimadzu-1700 UV spectrophotometer. Drug concentrations in the sample were determined from standard calibration curve. The release data were calculated by using PCP disso V3 software.

## Evaluation of sustained release matrix table

### Appearance

The tablets were observed visually and did not show any defect such as capping, chipping and lamination.

### Physical characteristic

The physical characteristic of (F1 to F9) such as thickness, diameter, hardness, friability, weight variation and drug content were determined and results of the formulations (F1 to F9) found to be within the limits specified in official books.

### Dimension (Thickness and Diameter)

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness and diameter can result in problems with packaging as well as consumer acceptance. The size (diameter) of the tablets of all formulations were found to be 8.0±0.0 mm and thickness ranged between 4.10±0.12 to 4.18±0.1.

### Tablet Hardness

The hardness of tablets was found to be in the range of 5.50±0.447 kg/$cm^2$ to 6.16±0.683 kg/$cm^2$. This indicates good tablet strength.

**Table 2: Physico-chemical characterization of Losartan potassium SRmatrix tablets**

| F Code | Dimension | | Hard ness (kg/$cm^2$)** | Friability (%)* | Weight variation (%)* | Drug content (%w/w)* |
|---|---|---|---|---|---|---|
| | Diameter (mm)** | Thickness (mm)** | | | | |
| F1 | 8.0±0.0 | 4.18±0.11 | 5.66±0.408 | 0.284±0.00 | 251.0±1.40 | 100.86±1.2 |
| F2 | 8.0±0.0 | 4.15±0.12 | 5.75±0.418 | 0.454±0.05 | 251.15±1.4 | 99.47±1.3 |
| F3 | 8.0±0.0 | 4.15±0.13 | 5.50±0.447 | 0.402±0.05 | 250.85±1.3 | 100.72±1.5 |
| F4 | 8.0±0.0 | 4.13±0.12 | 5.83±0.258 | 0.385±0.07 | 250.45±1.3 | 100.33±0.8 |
| F5 | 8.0±0.0 | 4.18±0.11 | 5.91±0.376 | 0.360±0.02 | 250.7±1.42 | 100.5±0.95 |
| F6 | 8.0±0.0 | 4.11±0.11 | 6.16±0.683 | 0.376±0.06 | 251.3±1.49 | 100.14±0.9 |
| F7 | 8.0±0.0 | 4.13±0.12 | 5.58±0.376 | 0.403±0.04 | 252.4±1.40 | 100.5±1.68 |
| F8 | 8.0±0.0 | 4.15±0.13 | 5.57±0.37 | 0.361±0.00 | 251.45±1.4 | 99.39±1.5 |
| F9 | 8.0±0.0 | 4.10±0.12 | 5.66±0.408 | 0.349±0.09 | 250.9±1.48 | 98.54±1.7 |
| Stan dards | - | - | 4-8 | <1 | 0.5 | 90-110 |

### Percent Friability

Percentage friability of all the formulations was found between 0.284±0.008 to 0.454±0.054%. This indicated good handling property of the prepared SR tablet.

### Weight Variation

A tablet is designed to contain a specific amount of drug. When the average mass of the tablet is 250 mg the Pharmacopoeial limit for percentage deviation is ± 5 %. The

percentage deviation from average tablet weight for all the tablet was found to be within the specified limits and hence all formulations complied with the test for weight variation according to the Pharmacopoeial specifications.

**Drug content of Losartan potassium**:

The content of active ingredients in the formulation was found to be between 98.54±1.7 to 100.86±1.2 % w/w,

***In-vitro* dissolution studies**

**Table 3: Dissolution data of formulation F1**

| Time (hours) | Dissolution medium | % Drug release* | cumulative % Drug release* | Amount (mg) | | % DEMDT |
|---|---|---|---|---|---|---|
| **0** | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| **0.5** | 0.1 N HCl | 2.31±0.74 | 2.34±0.79 | 1.17 | 1.17 | 0.25 |
| **1** | | 5.66±1.40 | 7.04±0.94 | 3.52 | 2.94 | 0.58 |
| **1.5** | | 7.76±0.94 | 8.01±0.66 | 4.01 | 4.47 | 0.66 |
| **2** | | 10.76±1.08 | 12.31±0.74 | 6.16 | 5.89 | 1.04 |
| **3** | | 9.97±0.67 | 24.1±0.60 | 12.05 | 5.89 | 1.50 |
| **4** | | 23.85±0.82 | 39.17±1.02 | 19.59 | 9.24 | 2.62 |
| **5** | pH 6.8 | 38.30±1.01 | 60.07±0.51 | 30.04 | 14.86 | 3.44 |
| **6** | phosphate bufffer | 57.78±1.18 | 71.03±1.08 | 35.52 | 21.26 | 3.83 |
| **7** | | 64.78±0.69 | 93.50±0.98 | 46.76 | 28.21 | 4.57 |
| **8** | | 69.77±1.56 | 99.15±0.47 | 49.57 | 35.23 | 4.78 |
| **9** | | 74.27±0.49 | 99.39±0.42 | 49.69 | 38.46 | 4.81 |
| **10** | | 76.83±0.98 | 99.78±0.39 | 49.89 | 40.04 | 4.82 |

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

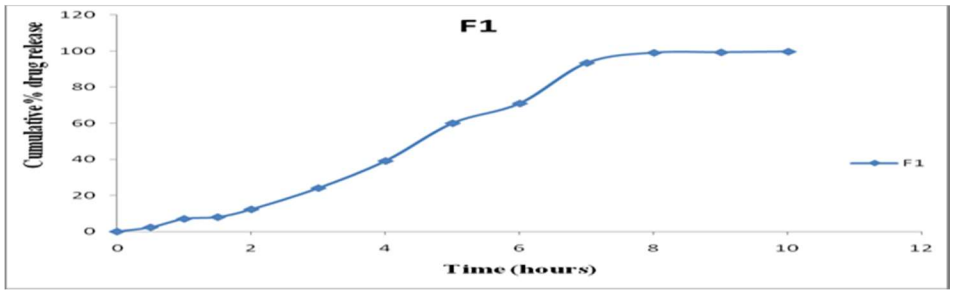


**Fig 1: Drug release profile of formulation F1**

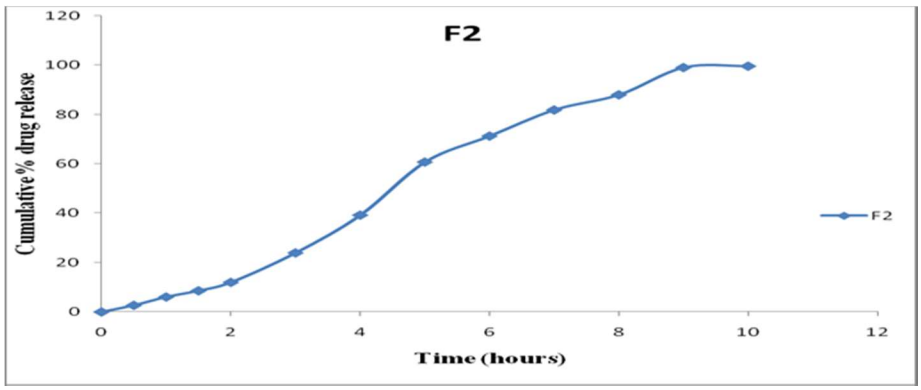


**Fig 2: Drug release profile of formulation F2**

**Table 4: Dissolution data of formulation F3**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | % DE | MDT |
|---|---|---|---|---|---|---|
| 0 | 0.1 N HCl | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | | 1.88±0.84 | 1.88±0.84 | 0.94 | 0.94 | 0.25 |
| 1 | | 5.87±0.76 | 5.87±0.76 | 2.94 | 2.41 | 0.59 |
| 1.5 | | 8.31±0.69 | 8.31±0.69 | 4.16 | 3.97 | 0.78 |
| 2 | | 11.13±0.89 | 11.13±0.89 | 5.57 | 5.41 | 1.03 |
| 3 | pH 6.8 phosphat e bufffer | 12.019±0.75 | 23.15±0.84 | 11.58 | 6.01 | 1.50 |
| 4 | | 27.362±0.68 | 38.49±0.85 | 19.25 | 9.43 | 2.62 |
| 5 | | 36.790±0.54 | 47.92±0.70 | 23.97 | 13.96 | 3.10 |
| 6 | | 47.971±0.42 | 59.10±0.51 | 29.56 | 18.70 | 3.66 |
| 7 | | 61.316±1.01 | 72.45±1.28 | 36.23 | 23.83 | 4.28 |
| 8 | | 67.714±0.52 | 78.85±0.70 | 39.43 | 28.92 | 4.58 |
| 9 | | 75.042±0.83 | 86.17±0.98 | 43.09 | 33.63 | 4.97 |
| 10 | | 85.316±0.75 | 96.45±0.97 | 48.23 | 38.29 | 5.51 |

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

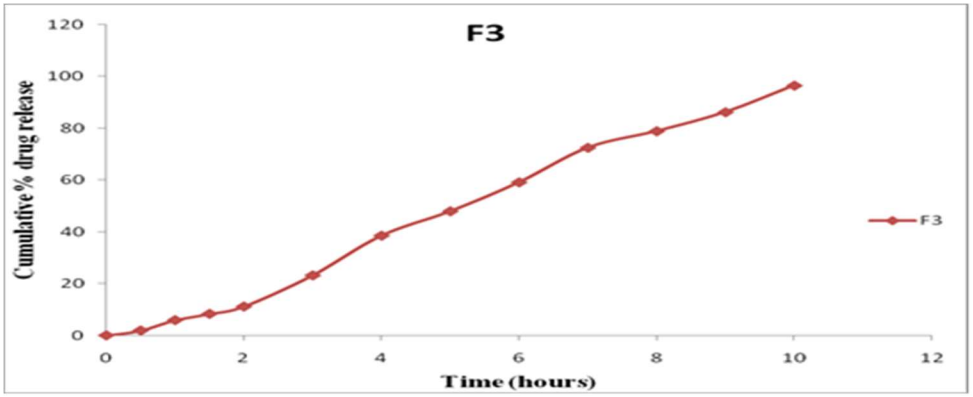


**Figure 3: Drug release profile of formulation F3**

**Table 5: Dissolution data of formulation F4**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | % DE | MDT |
|---|---|---|---|---|---|---|
| **0** | 0.1 N HCl | 0 | 0 | 0.00 | 0.00 | 0.00 |
| **0.5** | | 2.595±0.33 | 2.595±0.331.30 | | 1.30 | 0.25 |
| **1** | | 6.928±0.51 | 6.928±0.513.46 | | 3.03 | 0.56 |
| **1.5** | | 9.526±0.62 | 9.526±0.624.76 | | 4.76 | 0.75 |
| **2** | | 12.756±0.23 | 12.756±0.236.38 | | 6.36 | 1.00 |
| **3** | pH 6.8 phosphate bufffer | 39.81±0.61 | 40.303±0.7320.15 | | 19.91 | 1.50 |
| **4** | | 27.54±0.49 | 52.575±0.6826.29 | | 23.35 | 0.61 |
| **5** | | 47.27±0.32 | 60.030±0.4430.02 | | 26.16 | 2.23 |
| **6** | | 56.87±0.24 | 69.629±0.3534.82 | | 30.48 | 2.78 |
| **7** | | 74.59±0.84 | 87.352±0.9343.68 | | 35.52 | 3.67 |
| **8** | | 85.78±0.42 | 98.53±0.6149.26 | | 41.23 | 4.24 |
| **9** | | 86.12±0.26 | 98.87±0.4849.43 | | 42.87 | 4.37 |
| **10** | | 86.28±0.63 | 99.03±0.7649.51 | | 43.56 | 4.42 |

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

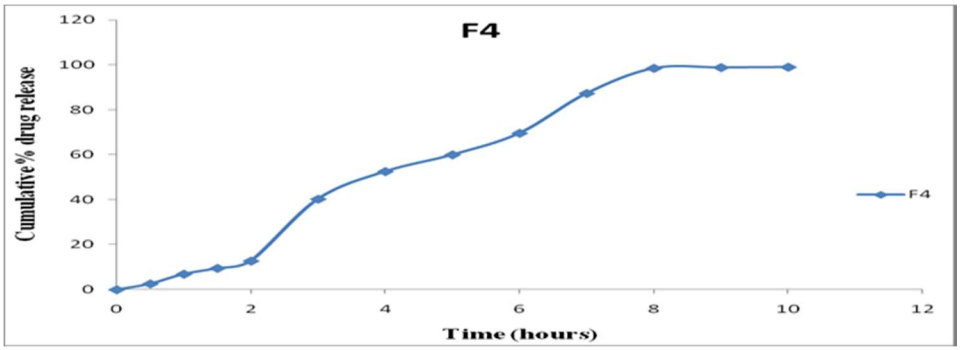


**Figure 4: Drug release profile of formulation F4**

**Table 6: Dissolution data of formulation F5**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | % DE | MDT |
|---|---|---|---|---|---|---|
| 0 | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | 0.1 N HCl | 3.02±0.66 | 3.02±0.66 | 1.51 | 1.51 | 0.25 |
| 1 | | 8.38±0.60 | 8.38±0.60 | 4.19 | 3.61 | 0.57 |
| 1.5 | | 11.51±0.56 | 11.51±0.56 | 5.76 | 5.72 | 0.75 |
| 2 | | 15.67±0.70 | 15.67±0.70 | 7.84 | 7.69 | 1.02 |
| 3 | pH 6.8 | 12.79±0.97 | 28.46±0.90 | 14.24 | 6.40 | 1.50 |
| 4 | phosphat e | 25.44±1.01 | 41.12±1.14 | 20.56 | 9.58 | 2.49 |
| 5 | bufffer | 38.82±0.65 | 54.50±0.86 | 27.25 | 14.09 | 3.19 |
| 6 | | 58.95±0.41 | 74.63±0.54 | 37.32 | 19.89 | 3.98 |
| 7 | | 67.47±0.66 | 83.15±0.90 | 41.48 | 26.08 | 4.29 |
| 8 | | 79.03±0.84 | 94.75±0.91 | 47.36 | 31.98 | 4.76 |
| 9 | | 83.37±0.75 | 99.04±0.48 | 49.52 | 37.52 | 5.02 |
| 10 | | 83.62±0.21 | 99.29±0.37 | 49.64 | 38.89 | 5.09 |

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

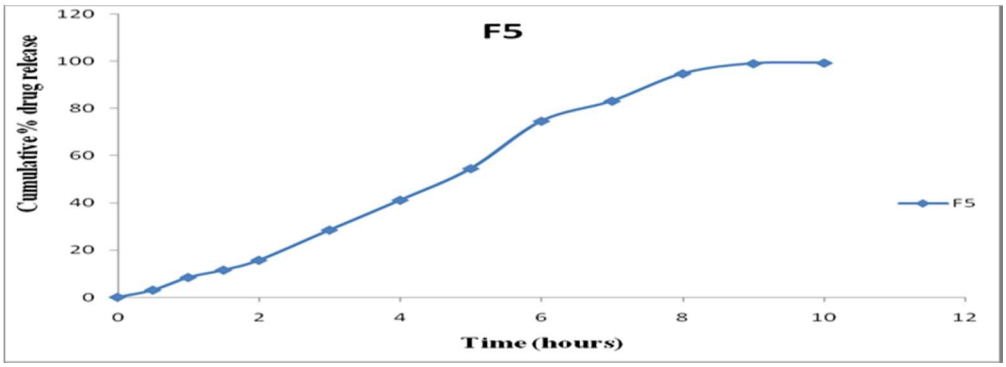


**Figure 5: Drug release profile of formulation F5**

**Table 7: Dissolution data of formulation F6**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | % DE | MDT |
|---|---|---|---|---|---|---|
| 0 | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | 0.1 N HCl | 2.132±0.56 | 2.132±0.56 | 1.07 | 1.07 | 0.25 |
| 1 | | 5.691±0.81 | 5.691±0.81 | 2.85 | 2.49 | 0.56 |
| 1.5 | | 10.31±0.34 | 10.31±0.34 | 5.16 | 4.33 | 0.87 |
| 2 | | 13.61±0.69 | 13.61±0.69 | 6.81 | 6.24 | 1.08 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | | 9.76±0.72 | 23.37±0.85 | 11.69 | 4.88 | 1.50 |
| 4 | | 24.07±0.81 | 37.68±0.99 | 18.85 | 7.89 | 2.69 |
| 5 | pH 6.8 | 36.45±0.99 | 50.06±1.12 | 25.04 | 12.36 | 3.30 |
| 6 | phosphate bufffer | 52.14±1.05 | 65.75±0.78 | 32.88 | 17.69 | 3.96 |
| 7 | | 61.36±0.78 | 74.98±1.53 | 37.49 | 23.27 | 4.35 |
| 8 | | 70.36±0.97 | 83.98±0.85 | 41.99 | 28.59 | 4.75 |
| 9 | | 81.94±1.01 | 89.98±0.90 | 47.78 | 33.88 | 5.28 |
| 10 | | 83.84±0.90 | 92.21±0.69 | 48.73 | 38.78 | 5.37 |

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

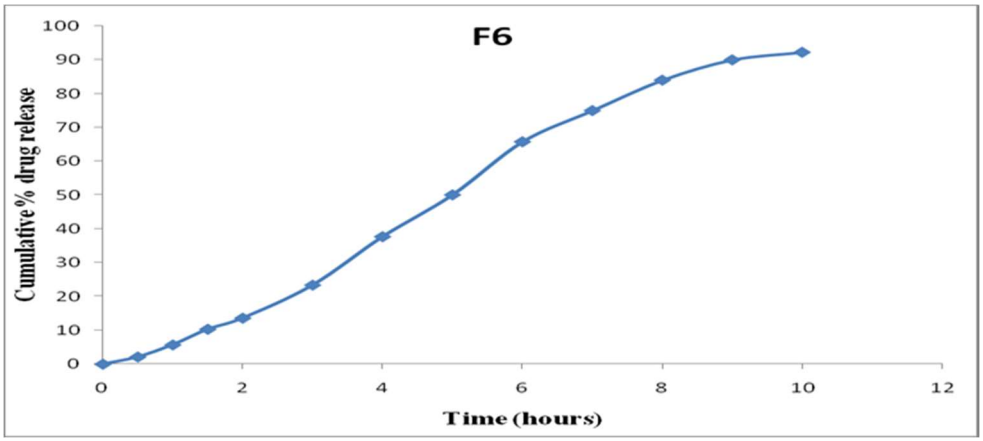


**Figure 6: Drug release profile of formulation F6**

**Table 8: Dissolution data of formulation F7**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | % DEMDT | |
|---|---|---|---|---|---|---|
| 0 | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | 0.1 N HCl | 3.366±1.57 | 3.366±1.57 | 1.68 | 1.68 | 0.25 |
| 1 | | 5.23±1.03 | 5.23±1.03 | 2.62 | 2.99 | 0.43 |
| 1.5 | | 9.79±0.78 | 9.79±0.78 | 4.90 | 4.50 | 0.81 |
| 2 | | 15.00±0.84 | 15.00±0.84 | 7.50 | 6.48 | 1.14 |
| 3 | | 12.51±0.88 | 27.51±0.70 | 13.76 | 6.26 | 1.50 |
| 4 | | 28.13±1.24 | 43.14±1.08 | 21.57 | 9.77 | 2.61 |
| 5 | | 47.49±0.69 | 62.50±0.57 | 31.25 | 15.38 | 3.38 |
| 6 | pH 6.8 | 57.56±0.84 | 72.56±0.74 | 36.28 | 21.57 | 3.75 |
| 7 | phosphate bufffer | 65.05±0.66 | 80.05±0.48 | 40.03 | 27.25 | 4.07 |
| 8 | | 69.92±0.59 | 84.92±0.43 | 42.46 | 32.28 | 4.31 |
| 9 | | 74.88±0.62 | 89.88±0.98 | 44.94 | 36.74 | 4.58 |
| 10 | | 76.59±1.54 | 91.59±1.23 | 45.8 | 40.64 | 4.69 |

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

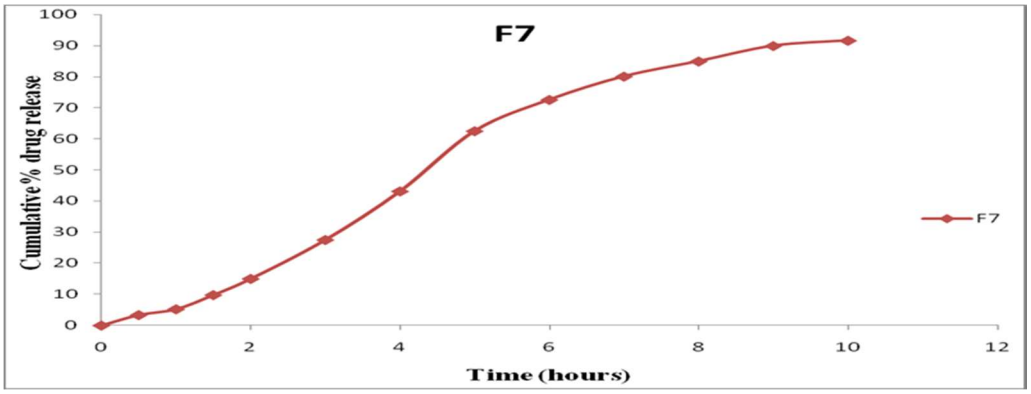


**Figure 7: Drug release profile of formulation F7**

**Table 9: Dissolution data of formulation F8**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | | % DEMDT |
|---|---|---|---|---|---|---|
| 0 | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | 0.1 N HCl | 2.872±1.07 | 2.872±1.07 | 1.44 | 1.44 | 0.25 |
| 1 | | 6.775±1.01 | 6.775±1.01 | 3.39 | 3.13 | 0.54 |
| 1.5 | | 9.095±1.28 | 9.095±1.28 | 4.55 | 4.73 | 0.72 |
| 2 | | 13.032±0.52 | 13.032±0.52 | 6.52 | 6.31 | 1.03 |
| 3 | | 14.12±0.65 | 27.15±0.97 | 13.58 | 7.06 | 1.50 |
| 4 | | 32.35±1.10 | 45.38±0.80 | 22.7 | 11.10 | 2.63 |
| 5 | pH 6.8 | 47.15±0.93 | 60.19±0.67 | 30.1 | 16.83 | 3.22 |
| 6 | phosphate bufffer | 59.35±0.48 | 72.38±0.33 | 36.2 | 22.91 | 3.68 |
| 7 | | 66.23±0.39 | 79.27±0.46 | 39.64 | 28.60 | 3.98 |
| 8 | | 72.41±1.09 | 85.44±0.63 | 42.73 | 33.69 | 4.28 |
| 9 | | 76.21±0.93 | 89.24±0.68 | 44.63 | 38.21 | 4.49 |
| 10 | | 79.44±1.05 | 92.47±0.57 | 46.24 | 42.17 | 4.69 |

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

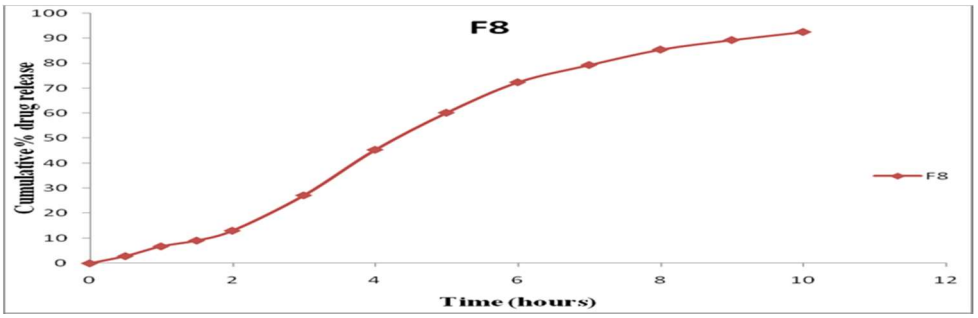


**Figure 8: Drug release profile of formulation F8**

**Table 10: Dissolution data of formulation F9**

| Time (hours) | Dissolution medium | % Drug release* | Cumulative % Drug release* | Amount (mg) | | % DEMDT |
|---|---|---|---|---|---|---|
| 0 | | 0 | 0 | 0.00 | 0.00 | 0.00 |
| 0.5 | 0.1 N HCl | 2.34±0.79 | 2.31±0.74 | 1.16 | 1.16 | 0.25 |
| 1 | | 7.04±0.94 | 5.66±1.40 | 2.83 | 2.57 | 0.55 |
| 1.5 | | 8.01±0.66 | 7.76±0.94 | 3.88 | 3.95 | 0.74 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2 | | 12.31±0.74 | 10.76±1.08 | 5.38 | 4.99 | 1.02 |
| 3 | | 11.77±0.58 | 20.74±0.84 | 10.37 | 5.28 | 1.50 |
| 4 | | 26.86±1.09 | 34.62±1.12 | 17.31 | 7.97 | 2.66 |
| 5 | pH 6.8 | 47.76±0.47 | 49.06±1.41 | 24.53 | 12.59 | 3.36 |
| 6 | phosphate bufffer | 58.72±1.03 | 68.54±0.98 | 34.27 | 18.50 | 4.08 |
| 7 | | 81.19±0.82 | 75.54±0.79 | 37.77 | 24.61 | 4.34 |
| 8 | | 86.84±0.26 | 80.53±0.56 | 40.27 | 29.95 | 4.57 |
| 9 | | 87.08±0.21 | 85.03±0.51 | 42.52 | 34.62 | 4.80 |
| 10 | | 87.47±0.20 | 87.60±0.77 | 43.8 | 38.71 | 4.96 |

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

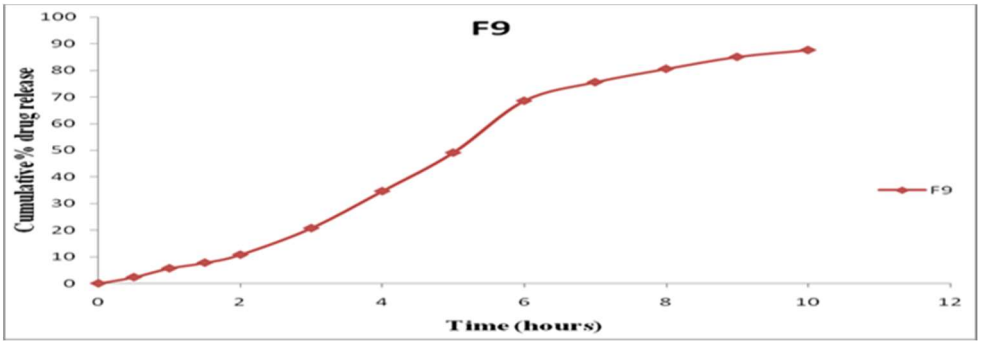


**Figure 9: Drug release profile of formulation F9**

The drug release data of dissolution studies of formulation (F1 to F3) containing xanthan gum is shown in Table 2, 3 and 4. The drug releases from formulation F1 to F3 containing xanthan gum at three concentration levels was found to be 99.78±0.39%, 99.67±0.69% and 96.45±0.97% respectively.

The drug release from formulation such as F4 to F6 containing Ethyl Cellulose at three concentration levels were found to be 99.03±0.76%, 99.29±0.37% and 92.29±0.69% respectively (Table 5, 6 and 7). While the drug release from formulation F7 to F9 containing HPMC K100M at three concentration levels were found to be 91.59±1.23%, 92.47±0.57% and 87.60±0.77% respectively (Table 8, 9 and 10).

When cumulative % drug release plotted versus time (Figure 4, 5 and 6), it was observed that, for three of the polymers used, an increase in polymer concentration induce a decrease in the release rate. The drug release rate from xanthan gum matrix was found to be less as compared to HPMC K100M. Whereas formulation containing ethyl cellulose(F4 to F6) gave higher drug release as compared to formulation containing xanthin gum (F1 to F3) and HPMC K100M (F7 to F9), which may be due to quick hydration of polymer matrix within 1 to 3 hours, after which matrix might get started to erode.

## SUMMARY AND CONCLUSION

Oral ingestion has long been the most convenient and commonly employed route of drug delivery due to its ease of administration, high patient compliance, least sterility constraints and flexibility in the design of the dosage form. Developing oral controlled release tablets for highly water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. Most of these highly water-soluble drugs, if not formulated properly, may readily release the drug at a faster rate and are likely to produce toxic concentration on oral administration. Hence, it is a challenging task to formulate a suitable dosage form for controlled delivery of highly water-soluble drugs. Losartan potassium, was chosen as a drug having high solubility. Losartanpotassium plays a major role in treating hypertension. It acts as an angiotensin antagonist.

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