WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 5, 755-762. Research Article ISSN 2277– 7105

FORMULATION AND COMPARATIVE EVALUATION OF SUSTAINED RELEASE TABLETS OF LEVOFLOXACIN USING DIFFERENT POLYMERS

Pavithra N., Haripriya S., Jibeen K., Akelesh T.* and Sam Johnson Udaya Chander J.

RVS College of Pharmaceutical Sciences, Sulur, Coimbatore.

Article Received on
13 Jan. 2018,

Revised on 03 Feb. 2018,
Accepted on 24 Feb. 2018

DOI: 10.20959/wjpr20185-11142

***Corresponding Author**
Dr. Akelesh T.
RVS College of Pharmaceutical Sciences, Sulur, Coimbatore.

ABSTRACT

Levofloxacin is a Fluoroquinoline antimicrobial drug. The aim of the study is to formulate and evaluate sustained release matrix tablets of levofloxacin, to reduce the side effects and improved patient compliance. In Levofloxacin the active component is race mate ofloxacin, is used in variety of clinical conditions that are sinusitis, lower respiratory tract infections, uncomplicated skin and soft tissues infections, urinary tract infections and bacterial conjunctivitis. By using HPMC, guar gum and xanthan gum, as polymer, microcrystalline as a filler and starch as a binder, prepared different batches of sustained release matrix tablets of levofloxacin by wet granulation method.

KEYWORDS: Levofloxacin, Sustained Release, HPMC, Polymer.

INTRODUCTION

Sustained Release Drug Delivery

Traditional drug delivery system has been characterized by immediate release and repeated dosing of the drug which might lead to the risk of dose fluctuation, this arises the need of a formulation with control release that maintain a near-constant or uniform blood level. Sustained release[1] with the introduction of extended release matrix tablet has proved to be an effective tool to control the release of drug without involving the complex production procedures.[2,3] By the sustained release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. The sustained release helps to achieve the following goals.[4,6]

i) Uniform release of drug over prolong period of time.

ii) Reduced dosing frequency.

iii) Less fluctuating blood levels.

Parameters for Drug to be formulated in Sustained Release Dosage form

There are some physicochemical parameters for the drug selection to be formulated in sustained release dosage form which mainly includes the knowledge on the absorption mechanism of the drug form the Gastro Intestinal (G.I.) tract, its general absorbability, the drug's molecular weight, solubility at different pH and apparent partition coefficient.[7,8] Hence, an attempt was made to formulate sustained release matrix tablets for the broad spectrum antibacterial agent levofloxacin.[9] This is to study the effect of nature of the polymer and drug: polymer ratio on the rate of drug release The present study was designed with the following objectives.[10]

1. Pre formulation studies to find out the compatibility between the drug and the polymer by FT-IR spectroscopy.
2. Preparation and characterization of granules.
3. Formulation of different batches of sustained release matrix tablets.
4. Evaluation of formulated tablets as per Pharmacopoeia standards

- Physicochemical characterization
- Uniformity of drug content
- *In vitro* drug release studies

5. Release kinetics studies.

MATERIALS AND METHOD

Preparation of levofloxacin tablets

Levofloxacin tablets are prepared by wet granulation method. The quantities of the levofloxacin and different polymers to be added to the granules such as HPMC, guar gum, xanthan gum, locust bean gum and Amorphophallus starch, Avicel PH 102, were weighed according to the formula given in Table and transferred in a mortar pestle and mixed thoroughly. The obtained powder mass were then mixed with 5% starch paste to obtain a sluggy mass. The mass was passed through sieve no 12 and the granules separated were dried at 40^{o}C for 4 h. The dried granules were screened through sieve no 22 and stored for further studies.

Table 1: Formulation trials.

Ingredients	Levo-floxacin (mg)	HPMC (mg)	Guar Gum (mg)	Xanthan Gum (mg)	Micro-crystalline cellulose (mg)	Starch Paste (mg)	Magnesium Stearate (mg)	Talc (mg)
X-1	100	-	-	-	191	q.s	6	3
X-2	100	40	-	-	151	q.s	6	3
X-3	100	80	-	-	111	q.s	6	3
X-4	100	120	-	-	71	q.s	6	3
X-5	100	150	-	-	41	q.s	6	3
X-6	100	180	-	-	11	q.s	6	3
X-7	100	-	40	-	151	q.s	6	3
X-8	100	-	80	-	111	q.s	6	3
X-9	100	-	120	-	71	q.s	6	3
X-10	100	-	150	-	41	q.s	6	3
X-11	100	-	180	-	11	q.s	6	3
X-12	100	-	-	40	151	q.s	6	3
X-13	100	-	-	80	111	q.s	6	3
X-14	100	-	-	120	71	q.s	6	3
X-15	100	-	-	150	41	q.s	6	3
X-16	100	-	-	180	11	q.s	6	3

qs = Quantity sufficient.

The dried granules obtained were taken and specified quantity of magnesium stearate and talc were added and mixed for the compression of tablets. An ideal mixture was directly punched into tablets weighing about 300 mg containing 100 mg of levofloxacin by Rotary tablet compression machine (12 stations, Karnavati, India), using 9 mm diameter concave punches. The different batches of levofloxacin tablets were collected and stored in air tight and light resistant containers.

Table 2: Physicochemical evaluation of levofloxacin tablets.

Batch code	Parameter			
	Hardness (Kg/cm^2)*	Friability (%)**	Weight variation (%)**	Drug content (%)***
X1	5.6±0.5	0.011±0.04	1.2±0.04	92.32±0.10
X2	7.3±0.02	0.015±0.020	1.5±0.05	83.5±0.20
X3	5.8±0.10	0.02±0.015	0.10±0.02	80.2±0.20
X4	7.9±.30	0.010±0.025	0.86±0.010	75.3±0.30
X5	6.4±0.20	0.005±0.015	0.09±0.025	97.43±0.20
X6	5.7±0.20	0.012±0.017	0.07±0.03	95 23±0.10
X7	5.6±0.30	0.26±0.025	0.93±0.015	93.12±0.15
X8	6.3±0.20	0.30±0.02	0.14±0.025	90.23±0.35
X9	4.9±0.10	0.32±0.025	0.256±0.033	85.62±0.25
X10	6.7±0.20	0.20±0.021	0.278±0.015	90.23±0.20
X11	7.3±o.10	0.15±0.015	0.292±0.005	87.23±0.33
X12	5.2±0.16	0.12±0.015	0.78±0.010	90.45±0.34
X13	6.2±.10	0.36±0.010	0.62±0.10	89.12±o.25
X14	5.3±0.20	0.35±0.025	0.56±0..2	88.45±0.20
X15	5.8±0.17	0.28±0.05	0.78±0.02	86.23±0.10
X16	4.1±0.15	0.33±0.07	0.89±0.05	93.18±0.05

Preparation of Solutions

In this levofloxacin tablet different type of buffer solution can be used for as:

- **Phosphate buffer (pH 6.8) solution**
- **Potassium dihydrogen phosphate (0.2 M) solution**
- **Sodium hydroxide (0.2 M) solution**
- **Acid Buffer (pH 1.2) Solution**

Design of Oral Sustained Release Drug Delivery System

The oral route administration is mostly adopted route because of its comfortable dosage form, design and patient care. Several parameters should be kept in mind before formulating sustained release dosage form which includes various pH in GIT, the gastrointestinal motility, the enzyme system and its effect on the dosage form and the drug. Most of sustained release dosage form follows the mechanism of diffusion, dissolution or combination of both, to produce slow release of drug at predetermined rate. Hypothetically, a sustained release dosage form should release the drug by a zero-order mechanism which maintains drug plasma level time similar to intravenous infusion. Plasma drug concentration profiles for conventional tablet or capsule formulation, a sustained release formulation and a zero order sustained release formulation are as follow in given figure 1.1.

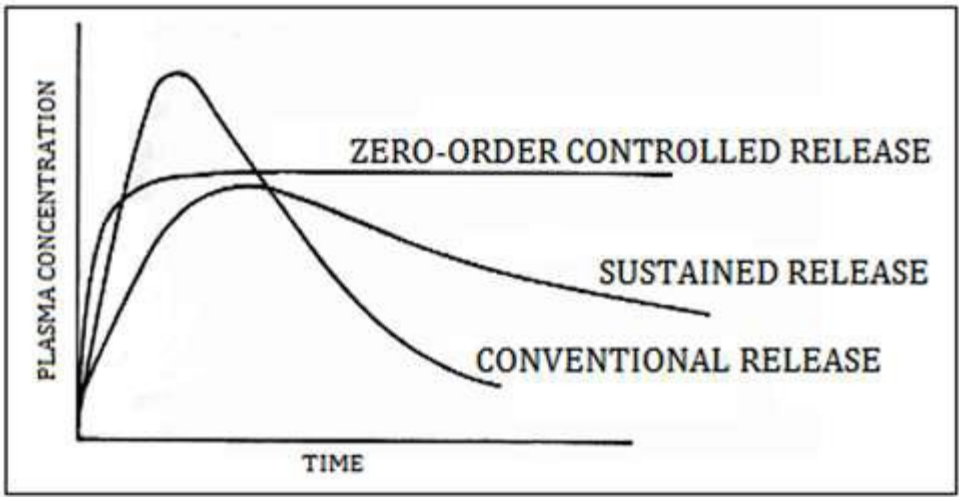

Figure 1.1: Plasma drug concentration profile for conventional release, a sustained release and zero order controlled release formulation.

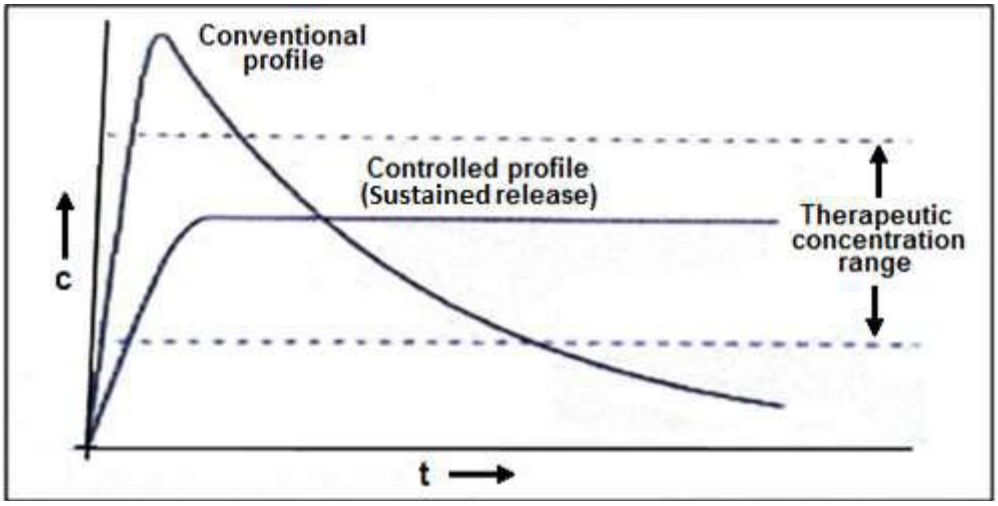

Figure 1.2: Comparison of conventional and controlled release profiles.

RESULTS

Preformulation study of active ingredient

a) Physicalstate: Levofloxacin is a light-yellowish-white to yellow-white crystal or crystalline powder.

b) Meltingpoint: 214-216°C

c) Solubility: Slightly soluble in water, soluble in glacial acetic acid, slightly soluble or soluble in dichloromethane, slightly soluble in methanol.

UV Scanning

a) Scanning of Levofloxacin in pH 1.2

The prepared solution of levofloxacin in pH1.2 HCl was scanned in UV spectrophotometer and λ_{max} was found to be 293 nm.

b) Scanning of Levofloxacin in pH 6.8 phosphate buffer

The prepared solution of levofloxacin in pH 6.8 phosphate buffer was scanned in UV spectrophotometer and λ_{max} was found to be at 293 nm.

DISCUSSION

Preparation of levofloxacin tablets

Wet granulation method is mainly used for the preparation of levofloxacin matrix tablets. Because of good drug release profile and cost effective the hydrophilic matrix systems are widely used for the preparation of oral sustained drug delivery. In hydrophilic polymer matrix system, it consists of hydrophilic polymer, drug and other excipients distributed throughout the matrix system.

Characterization of Levofloxacin tablets

Pre compression parameters

The pre compression studies are used for identifying the good flow property of the granules and thus give homogenous filling of dies. The pre compression parameters are angle of repose, bulk density, tapped density and compressibility index.

percentage yield : 91.73 to 98.12%

Bulk density : 0.412 to 0.493 gm/ml

Tapped density : 0.456 to0.579 gm/ml

Compressibility index : 8.90 to 13.67

Mean particle size : 0.492± to0.664±0.15

Angle of repose : 28.12±0.16 ^{o} to 30.90±0.22^{0}

CONCLUSION

Levofloxacin is one of the most widely used fluoroquinolones. Designing a sustained release formulation for the drug levofloxacin may improve the efficacy of drug and patient compliance. It prolongs therapeutic concentration of drug in the blood and decrease the frequency of dosing and hence, an attempt was made to formulate a sustained release matrix tablet for the broad spectrum antibacterial agent levofloxacin for increased margin of safety and better therapeutic control.

The main objective of the study was to develop sustained release matrix tablets of levofloxacin and compare their release. The study led the following conclusions:

- The drug levofloxacin was selected for the study, because of its proved activity and better clinical applications.
- The pre formulation FT-IR studies revealed that there was no interaction between the drug levofloxacin and the polymer HPMC, guar gum and xanthan gum.
- The physicochemical parameters of the prepared granules observed support the ideal flow nature of the formulated granules.
- The physicochemical parameters of the prepared tablets comply with the official standards.
- The effect of drug to polymer ratio on the *in vitro* drug release behavior was significant. Formulation X4, X10 and X14 showed better sustained release when compared to other batches and this shows the ideal drug, polymer and excipients combination. From these formulations X4 was found to be better released than X10 and X14.

- Release of drug from the tablets was first order diffusion controlled as indicated by higher R^2 values in first order and Higuchi kinetic model. Then, value of Korsemeyer-Peppas equation indicated that the release mechanism was non-Fickian.

Based on the observations, it can be concluded that the formulated sustained release matrix tablets of levofloxacin using widely accepted safe polymers and other excipients was capable of exhibiting sustained release properties. They are thus may be reducing the dose intake, minimize the blood level oscillations, dose related adverse effects and cost and ultimately improve the patient compliance and drug efficiency.

REFERENCES

1. Bhowmik D, Kumar KPS, Dutta A, Paswan S. "Trends in scope and opportunities of control release oral drug delivery systems". *Critical review in pharmaceutical sciences*, 2012; 1: 20-33.
2. Vamsy KA, Srinath KR, Chowdary PC. "Formulation development and evaluation of Divalproex sodium extended release tablet". *International Journal of Research pharmaceutical and Biomedical Science*, 2011; 2: 809-832
3. Patel H, Panchal DR, Patel U, Brahmbhatt T. "Matrix Type Drug Delivery System: A Review". *JPSBR*., Nov-Dec 2011; 1(3): 143-151.
4. Kumar KPS, Bhowmik D, Srivastava S. "Sustained Release Drug Delivery System Potential". *The Pharma Inovation*., 2012; 1(2): 48-60.
5. Lee TW and Robinson JR, "In Remington: The science and practice of pharmacy, Gennaro", 20th edition, *Baltimore, Lippincott Williams and Wilkins*, 2000; 903-929.
6. Ansel HC, Allen LV, and Popovich NG, "Pharmaceutical dosage forms and drug delivery system", 9th edition, *Lippincott William & Wilkins*, 2005; 257-271.
7. WWW.fda.gov
8. Chauhan MJ, Patel SA. "A Concise Review on Sustained Drug Delivery System and Its Opportunities". *Am. J. Pharm Tech Res*., 2012; 2(2): 227-238.
9. Onlinelibrary.wiley.com
10. Ho WH, and Lee VHL, "Influence of drug properties on design", *Controlled Drug Delivery Fundamentals and Applications, Marcel Dekker*, 2nd edition, New York, 1987; 16-25.
11. Gemma Vilar, Judit Tulla Puche, Fernando Albericio, (2012) "Polymers and drug delivery systems" *Current drug delivery*, 9: 000-000.

12. Sarika Pundir, Ashuthosh Badola, Deepak Sharma, (2013) "Sustained release matrix technology and recent advance in matrix drug delivery system: A review" *International journal of drug research and technology*, 3(1): 12-20.
13. V.T.Thakkar, P.A.Shah, T.G.Soni, (2009) "Goodness-of-Fit Model-Dependent Approach for Release Kinetics of Levofloxacin Hemihydrates Floating Tablet" Dissolution tech, 2009.