



INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

EFFECT OF DIFFREENT GRADES OF HPMC ON FORMULATION DEVELOPMENT AND IN-VITRO CHARACTERIZATION OF GASTRORETENTIVE DELIVERY SYSTEM OF LOSARTAN POTASSIUM

KAPOOR D¹, NAGARIA K², LAD C¹, PATEL M¹, SWAPNIL SHARMA³

1. Dr. Dayaram Patel Pharmacy College, Sardarbaug, Station Road, Bardoli, Surat, Gujarat, India.
2. Associate Scientist, Cadila Pharmaceutical Ltd., Ahmedabad, Gujarat.
3. Department of pharmacy, banasthali university, banasthali, Rajasthan.

Accepted Date: 06/11/2013; Published Date: 27/12/2013

Abstract: Rapid gastrointestinal transit could result in incomplete drug release from the drug delivery system above the absorption zone leading to diminished efficacy of the administered dose. Hydrodynamically balanced system (HBS) or Floating tablets has gained importance in recent days to improve absorption of drugs especially those that are absorbed from stomach and small intestine. In the present study, an attempt was made to fabricate and characterize an HBS dosage form of losartan potassium tablet. The different viscosity grades of Hydroxypropylmethyl cellulose polymer like HPMC K100, HPMC K4M, HPMC KV600, HPMC K50 was incorporated as hydrophilic swellable polymers for preparing matrix-floating tablets. Sodium bicarbonate was incorporated as a gas-generating agent. The prepared floating tablets were evaluated for the physical parameters like thickness, hardness, friability, drug content, floating lag time, floating time and *In-vitro* dissolution studies. The mechanism of drug release was anomalous type and depends upon the viscosity of polymers, which was mainly concluded as the major controlling factor for the drug release. The results showed that the formulation containing active pharmaceutical ingredient: HPMC KV600 in the ratio of 1: 0.5 is suitable for the formulation of gastroretentive floating tablets of losartan potassium.

Keywords: Losartan potassium, Hydroxypropylmethylcellulose, buoyancy lag time, Matrix Floating tablet, bioavailability studies, and accelerated stability studies.



PAPER-QR CODE

Corresponding Author: MR. D. KAPOOR

Access Online On:

www.ijprbs.com

How to Cite This Article:

Kapoor D, IJPRBS, 2013; Volume 2(6): 210-217

INTRODUCTION

One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time by using gastro-retentive dosage forms (GRDFs). It remains in the gastric region for several hours and hence prolongs the gastric residence time of drug. It has several advantages over immediate release dosage form including the minimization of fluctuations in drug concentration in plasma and at the site of action over prolonged periods of time, resulting in optimized therapeutic efficiencies and reduce the side effect, reduction of total dose administered and reduction of administration frequency leading to improved patient compliances^{1,2} Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms.

Floating tablets are gastro-retentive drug delivery systems based on non-effervescent approach. These microspheres are characteristically free flowing powders having a size less than 200 μm and remain buoyant over gastric contents and for prolonged period. As the system floats over gastric contents, the drug is released slowly at desired rate resulting in increased gastric retention with reduced fluctuations in plasma drug concentration.^{3,4}

Losartan potassium is an orally active non-peptide angiotensin-II receptor antagonist. It is the first of a new class of drug to be introduced for clinical use in "hypertension" due to selectively blockade of AT 1 receptors and consequent reduced pressure effect of angiotensin II. It belongs to class III is soluble in acidic pH. Losartan having narrow therapeutic index, poor bioavailability (25 to 35%) and short biological half life (1.5 2hrs). Conventional tablets should be administered 3 to 4 times to maintain plasma drug concentration. Administration of Losartan potassium in a floating drug delivery system would be more desirable for antihypertensive effects by maintaining the Losartan plasma concentration well above the minimum effective concentration. Developing a sustained release drug delivery system like floating tablet for Losartan potassium is desirable for an effective treatment of hypertension and is useful to reduce the dosage frequency to improve patient compliance.^{5,6,7,8,9}

Material & Methods:

Materials:

Active pharmaceutical ingredient:

Losartan potassium was a gift sample from Aurobindo Pharma Ltd, Hyderabad

Polymers & Reagents:

PVP K-30 ,HPMC KV600, HPMC K100M, HPMC K50M, HPMC K4M, Iso propyl alcohol and PEG-6000 were received as gift sample from Cadila pharma, India. Magnesium Stearate and talc from S.D. fine chemicals Pvt. Ltd. Sodium bicarbonate was procured from Signet Chemicals. All other ingredients used were of analytical grade.

Preparation of HBS Tablets:

The active pharmaceutically ingredient losartan potassium , HPMC of various grades, poly ethylene glycol 6000, Sodium bicarbonate, were passed through mesh 40# separately and blended thoroughly. The wet mass was passed through sieve 16# and dried at 65°C for one hour to get the moisture content less than one. The blend was granulated with PVP K-30 in IPA solution. Magnesium Stearate and talc were passed through sieve 40# and blended with dried granules. The lubricated granules were compressed on Cadmach eight punch tablet machine. (Table 1)

Table 1: Formulation parameters for gastro retentive floating tablet of losartan potassium

S.No	Ingredients	Amount (mg/tablet)
01.	PEG-6000	60
02.	Sodium bicarbonate	90
03.	PVP K-30	90
04.	Lactose	90
05.	Magnesium stearate	10
06.	Talc	10

HPMC of various grades used with drug in the ratios (Drug: Polymer, (1:1, 1:1.5, 1:0.5).

Characterization of gastro retentive floating tablet of losartan potassium:

The compatibility study between ingredients was performed by IR spectral analysis. The granules were evaluated for its flow properties and compressibility studies by measuring the angle of repose and Carr's index. The formulated floating tablets were evaluated for the following physical characters like thickness, hardness, friability, drug content, floating lag time, floating time and dissolution profile. The results were presented in the Table 2. The best

formulation was chosen on the basis of and buoyancy lag time, floating time and dissolution profile.^{10, 11}

***In-vitro* buoyancy studies:**

The *in vitro* buoyancy was determined by the floating lag time. The tablets were placed in 100-mL beaker containing 0.1N HCl (P^H 1.2). The time required for the tablet to rise to the surface for floating was determined as the floating lag time and further floating duration of all tablets was determined by visual observation.^{10, 11}

***In-vitro* dissolution study:**

The release rate of losartan potassium from floating tablets was determined using *United States Pharma-copeia (USP)* 24 Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl, at 37±0.5°C and 75 rpm. A sample (5 ml) of the solution was with-drawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45 μ membrane filter and diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 254 nm using a UV/Vis double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.¹²

Result and discussion:

Losartan potassium raw material passed all the tests for identification and percentage of purity of Losartan potassium was found to be 97.65%. The physical compatibility test between drug and other tablets was carried out at 25-30°C and 75% R.H for two months. The mixture does not show any visible change, and thus inferring that drug and other components do not have any physical incompatibility. The FTIR and UV scan of the gastroretentive tablets of losartan potassium exhibited similar peaks to that of the pure drug. No interactions were detected, hence confirming the suitability of excipients used in the formulation.

The bulk density and tapped density ranged from 0.435 to 548 and 0.519 and 0.634 respectively. The percentage compressibility index was below 30, indicating good flow properties. All the granules FLT1 to FLT6 were found to be free flowing and their angles of repose were below 30.

The physical properties of FLT1 to FLT6 such as tablet size, hardness, friability and weight variation were determined and results are shown in Table 2 and results are found to be within the limits specified in Pharmacopoeia. The best formula should possess the minimum lag time (within few minutes) as well as maximum floatation time (more than 12h). Buoyancy lag time and duration of floating were determined using USP dissolution test apparatus and the results

were represented in Table 2 and Figure 1 respectively. Buoyancy lag time of tablet FLT3 was 06 seconds i.e. less than one minute which is the least value as compared to other tablets. The floating time of FLT3 was also found to be 24 hours.

Table 2: Physical parameters of gastro retentive floating tablets of losartan potassium

Ingredients (mg)	FLT1	FLT2	FLT3	FLT4	FLT5	FLT6
Thickness (mm)	5.72	6.81	4.32	6.17	7.01	4.58
Hardness (Kg/Cm ²)	4.2	3.9	3.6	4.1	4.2	3.8
Lag Time(Sec)	12	16	06	10	13	18
Flotation time (Hours)	24	24	24	24	24	24
% Weight Loss	0.054	0.045	0.030	0.042	0.052	0.010
Drug Content (Mean±SD)	251.7±2.22	250.8±2.11	248.1±1.32	245.9±1.65	247.4±1.36	252.9±1.67
Friability	0.641±0.01	0.453±0.05	0.514±0.02	0.443±0.02	0.613±0.04	0.576±0.05

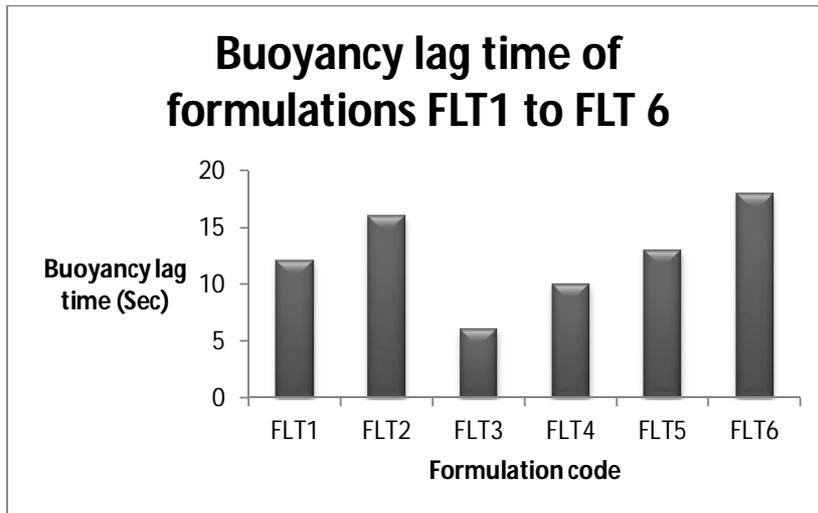


Figure 1: Buoyancy lag time of formulations FLT1 to FLT6

The dissolution studies of the formulations FLT1 TO FLT 6 were represented in Figure 2. The percentage drug release of the formulation F-II, F-V, F-VIII, FXI was below 50%. Where as for formulation F-I, FIV, F-VII, F-X were below 70%. The formulation FLT3 showed a constant release of 99% in a sustained manner as similar to zero order kinetics. (Figure 3)

Suitability of HPMC grades is given in the order of :

HPMC KV600>HPMC K4M > HPMC K100>HPMC K50

concluded by different dissolution profiles.

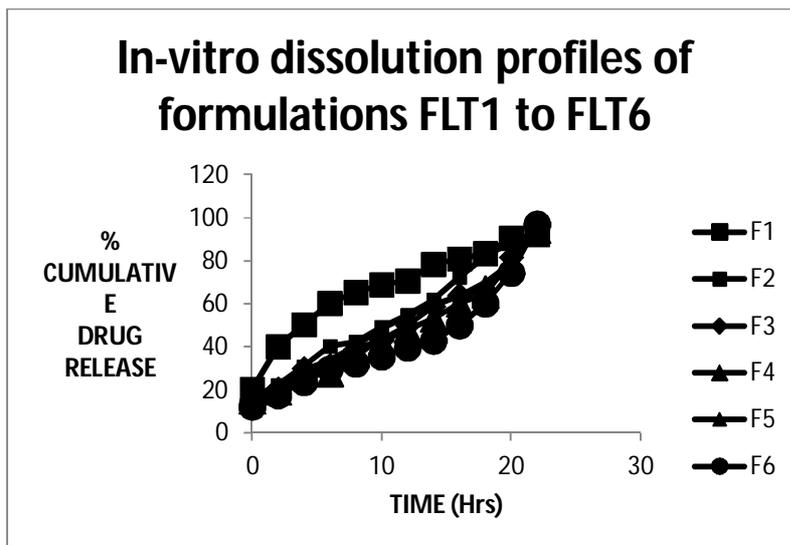


Figure 2: In-vitro dissolution profiles of formulations FLT1 to FLT6

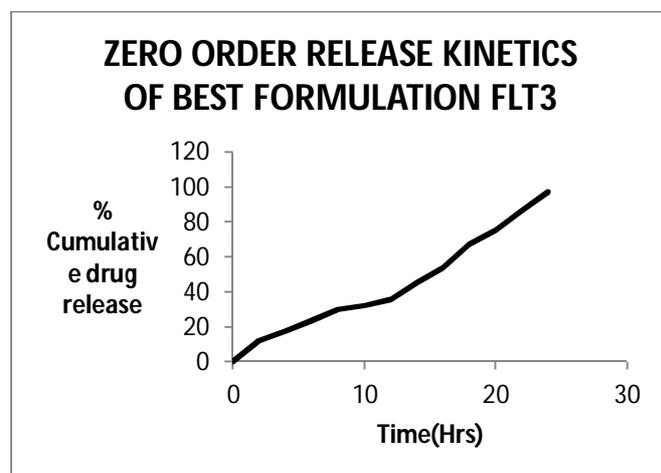


Figure 3: Zero order release kinetics of best formulation FLT3

7. Conclusion:

Gastro retentive floating tablets of losartan potassium were prepared by direct compression method. The tablets were prepared with acceptable hardness, consistent weight uniformity and low tablet friability. It can be concluded that gastroretentive floating tablets of losartan potassium FLT3 with HPMC KV600 in the ratio of 1:0.5 shows desirable characteristics of *In-vitro* floatability of 24 hours and invitro release of 96.98% over a period of 24 hours, with zero order kinetic release and hence FLT3 was chosen as best formulation. *In vitro* release data were fitted to various kinetic models and drug release predominantly follows non-Fickian diffusion. Overall, this study concludes that viscosity is a major factor affecting the drug release and floating properties of FDDS.

References:

1. Chien YW; Novel drug delivery system. 2nd ed; Vol. 50, Marcel Dekker Inc., New York, 1992, 161- 172.
2. Khar RK, Vyas SP.; Targeted and controlled drug delivery novel carrier system, 1st ed.; CBS Publishers and Distributors, New Delhi, 2002, 417- 441.
3. Arora S, Ali J, Ahuja A, Khar Roop K. and Baboota S, Floating Drug Delivery Systems: A Review, AAPS PharmSciTech, 2005, 6 (3), 372-390.
4. Tanwar Y. S.; www.pharmainfo.net, 4(3), 2006.

5. Brunton LL, Johns L, Parker KL. "Goodman & Gilman's. "The Pharmacological Basis of Therapeutics 11th edition". Mc graw hil education pvt.ltd; New Delhi. 2006; 546-562.
6. Prajapati BG and Patel KR. Once-Daily Sustained-Release Matrix Tablets of Losartan potassium: Formulation and *In Vitro* Evaluation. Int J Medical and Clinical Res 2010; 1(1): 1-7.
7. Drug information for Losartan potassium from United States Pharmacopoeia, 2007, USP29-NF 24, page 1280.
8. Drug information for Losartan potassium from Indian pharmacopoeia.2010; 2: 1607-1608.
9. Rang and Dale, Hormones, Text Book of Pharamacology, 5th Edition, edited by Laurence Hunder, 2004, page 385.
10. Jaimini M, Rana AC, Tanwar YS. Formulation and Evaluation of Famotidine Floating Tablets, Current Drug Delivery, 2007, 4, 51-55.
11. Cooper J, Gunn C. "Powder flow and compaction", In: Carter SJ, eds. Tutorial Pharmacy. New Delhi, India: CBS Publishers and Distributors; 1986; 211-233.
12. Higuchi T. Mechanism of rate of sustained action medication. J Pharm Sci., 1963, 52:1145-1149.
13. Peppas NA, Sahlin JJ. A simple equation for the description of solute release III. Coupling of diffusion and relaxation. Int J Pharm, 1989, 57,169-17.
14. Rosa M, Zia H, Rhodes T. Dosing and testing in vitro of a bioadhesive and floating drug delivery system for oral application. Int. J. Pharm., 1994,105, 65-70.
15. Talukder R, Fassihi R, Jain NK. A new approach in gastro retentive delivery systems Drug . Dev. Ind. Pharm, 30(4), 405-412.
16. Jaimini M, Tanwar YS, Srivastava B. Formulation and characterization of gastroretentive delivery system of losartan potassium, International Current Pharmaceutical Journal 2012, 2(1): 11-17.