ejpmr, 2016,3(9), 529-533

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 3294-3211

EJPMR

OPTIMIZATION OF MATRIX TABLETS CONTAINING ALFUZOSIN HCL EMPLOYING HPMC K4 M

B. Srinivasa Rao*[1], Prof. J. Vijayanratna[1], Ch. Taraka Ramarao[2]

1. Department of Pharmaceutical Technology Sri Venkateswara College of Pharmacy, Etcherla, Srikakulam, Andhra Pradesh, INDIA-532410.
2. AU. College of Pharmaceutical Sciences, Andhra University, Visakha Patnam.

***Correspondence for Author: B. Srinivasa Rao**

AU. College of Pharmaceutical Sciences, Andhra University, Visakha Patnam.

Article Received on 19/07/2016 **Article Revised on 08/08/2016** **Article Accepted on 29/08/2016**

ABSTRACT

The present investigation involves HPMC K4M was gastro retentive drug delivery systems of alfuzosin HCl using HPMC K4M is the matrixing agent and floating enhancer. The Sodium bicarbonate in the acidic environment reacts with the acid and produces carbon dioxide. The gastro retentive tablets can be formulated to increase the gastric residence time and there by increase the oral bioavailability. From the drug release study it was concluded that the AFTA5 formula of HPMC K4 M matrix tablets have given the controlled release up to 12 hours by showing increased release with floating lag time 29 seconds. Non – Fickian diffusion was the drug release mechanism from the matrix tablets formulated employing HPMC K4 M. The matrix tablets (AFTA5) formulated employing 50 % HPMC K4 M are best suited to be used for gastro retentive dosage form of Alfuzosin HCl. Finally, it can be concluded that good candidates for the preparation of gastro retentive dosage forms due its gastric stability, gastric absorption, less bioavailability.

KEYWORDS: Floating, Lag time, HPMC K4 M, Sodium bi carbonate, GFDDS.

1. INTRODUCTION

Alfuzosin HCl is an alpha-adrenergic receptor blocker, highly soluble in water it has bioavailability of 49% while the corresponding value under fasting condition is around 25%. This shows that food has a significant impact on the oral absorption of alfuzosin, potentially through the prolongation of gastric residence and having absorption in proximal intestine. Which is used in treatment of benign prostatic hyperplasia. The present study also aims to develop a floatable drug delivery system of alfuzosin HCl that can enhance its bioavailability and can result in its site-specific delivery to the proximal small intestine.

Hence in the present investigation, it is aimed to develop GFDDS of alfuzosin HCl (effervescent floating tablets) with three different grades of hydroxy propyl methyl cellulose (HPMC). The GFDDS of the present investigation are designed to retain in the stomach for longer period of time and deliver the alfuzosin HCl effectively. The system provides increased absorption of the alfuzosin HCl at a rate such that effective plasma levels can be achieved and maintained for a prolonged duration. The pharmaceutical composition in the form of tablets comprises an effervescent agent and a swellable polymer. Upon contact with gastric fluids, the polymer forms a hydrated gel matrix and entraps the gas generated by the effervescent agent[3]. Thus, the combination of the effervescent agent and the swellable polymer permit the system to float in the stomach and act as a gastric retentive controlled drug delivery system. This system provides more reliable retention for prolonged periods of time compared to other gastric retention systems. The polymer HPMC K4M in different concentrations were employed to study the effect of molecular weight or viscosity on floating properties and drug release kinetics[4]. A gas generating agent sodium bicarbonate was used. Matrix tablets of alfuzosin HCl containing various proportions of polymers were prepared by wet granulation using isopropyl alcohol as a binder and were evaluated to design gastro retentive oral matrix tablets of alfuzosin HCl.

2. MATERIALS AND METHOD

Alfuzosin HCl (Ajantha pharmaceuticals, Mumbai)
HPMC K4 M (Orchid health care, Chennai)
Micro crystalline cellulose (Moly chemicals)
Sodium bicarbonate (Finar chemicals limited, Ahmedabad)
Hydrochloric acid (Fisher scientific)
Polyvinyl pyrrolidine (Moly chemicals)
Isopropyl alcohol (Finar chemicals limited, Ahmedabad)
Micro crystalline cellulose (Moly chemicals)
Magnesium stearate (Moly chemicals)

Talc (Cheminova private limited)
All other materials used were of Pharmacopoeial grade.

2.1 METHOD PREPARATION OF TABLETS
Matrix tablets each containing 10 mg of alfuzosin HCl were prepared in different proportions of drug and polymer as per the formulae given in Table.1. The required quantities of medicament and matrix materials were mixed thoroughly in a glass mortar by following geometric dilution technique. Isopropyl alcohol (1.5%) solution was added and mixed thoroughly to form dough mass. The mass was passed through Seive. No. 12 to obtain wet granules. The wet granules were dried at 60^0C. The dried granules were passed through Seive. No. 16 and mixed with sodium bicarbonate and lubricated with magnesium stearate (1%) and talc (1%). They were then passed through mesh No. 100 just 4-5 min before compression and blended in a closed polyethylene bag. The tablet granules were compressed into tablets on a rotary multi- station punching machine (Cadmach Machinery Co. Pvt. Ltd., Mumbai) to a hardness of 4-6 kg/sq.cm using 8 mm punches.

2.2 Evaluation of Prepared Tablets
2.2.1 Weight Variation

2.2.2 Hardness
The hardness of the matrix tablets prepared was tested using a Monsanto Hardness Tester.

2.2.3 Friability
For each formulation, the friability of tablets was determined using Roche Friabilator, respectively[3].

2.2.4 Floating lag time
The in vitro buoyancy was determined by floating lag time as per the method described by Rosa et al[3]. The tablets were placed in a 100-mL glass beaker containing simulated gastric fluid (SGF), pH 1.2, as per USP. The time required for the tablet to rise to the surface and float was determined as floating lag time[1].

2.2.5 Estimation of Alfuzosin in tablets
Five tablets were accurately weighed and powdered. Tablet powder equivalent to 10 mg of medicament was taken into 10 ml volumetric flask and 5 ml of 0.1N HCl was added. The mixture was shaken thoroughly for about 3mins. The solution was subsequently diluted suitably with simulated gastric fluid of pH 1.2 and assayed for alfuzosin HCl at 244 nm. Four samples of tablet powder were analyzed in each case.

2.2.6 Drug release study
Alfuzosin HCl release from matrix tablets prepared was studied using 8 station dissolution rate test apparatus (Lab India, Disso 2000) employing a paddle stirrer at 50 rpm and at 37± 0.5^0C by using 0.1N hydrochloric acid (900 ml) was used as dissolution fluid[2,3]. A sample (5ml) of solution was withdrawn ever hour up to 12 hrs and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter and diluted to suitable concentration with 0.1N hydrochloric acid. The absorbances of these solutions were measured at 244 nm using Elico UV SL-210 UV/VIS double beam spectrophotometer.

2.2.7 Data analysis: The drug release data were analyzed as per Zero Order, First Order, Higuchi and Peppas equation models to assess the drug release kinetics and mechanism from the matrix tablets prepared[1,6].

3. RESULTS AND DISCUSSION
Matrix tablets each containing 10 mg of alfuzosin HCl could be prepared employing HPMC K4M in different proportions (10%, 20%, 30%, 40%, 50%). The Hardness of the tablets was in the range of 4-6 kg/sq.cm. The weight loss in the friability test was less than 0.48 % in all the cases. All the matrix tablets prepared contained 98±2.5% of the labeled claim. All the tablets were found to be non- disintegrating in acidic pH 1.2. As such, the prepared tablets were of good quality with regard to drug content, hardness and friability. As the tablets formulated were non-disintegrating in acidic and alkaline fluids, they are considered suitable for a gastro retentive drug delivery system. Alfuzosin HCl release from the matrix tablets prepared was studied in 0.1N hydrochloric acid for 12hrs. The drug release profiles of alfuzosin HCl matrix tablets are given in Table.3 and shown in Fig1, Fig.2, Fig.3 and Fig.4. The drug release parameters are summarized in Table 5. Alfuzosin HCl release was relatively rapid in the case of matrix tablets prepared employing 10% HPMC K4M. The floating lag time of 35sec and a floating time of 1h 101.53% for drug release were observed for these tablets (Table.2). When 20% of HPMC K4M was used in the formula, the release at the end of the 4^{th} hour was about 99.09%. The matrix tablets containing 30% HPMC K4M released 100.58% drug at the end of the 8^{th} hr while the matrix tablets having 40% HPMC K4M released 101.08% at the end of the 9^{th} hr. The matrix tablets having 50 % of HPMC K4M showed minimum release of just 98.04% at the end of the 10^{th} hr.

The *in vitro* buoyancy with maximum floating lag time was 35 seconds. All the tablet formulations remained buoyant less than for 12 hours in SGF of pH 1.2.

The drug release data were analyzed as per Zero order, First order, Higuchi, Erosion and Peppa's equation models. The correlation coefficient (r) values in the analysis of the release data as per different kinetic models are given in Table.5. The analysis of release data as per zero order and first order kinetic models indicated that the alfuzosin HCl release from the matrix tablets followed Zero order kinetics. The correlation coefficient (r) values were higher in the zero order model than in the first order model. The plots of percent release versus square root of time were found to be linear with r values greater than 0.9. Hence it was concluded that with all the tablets prepared drug release was diffusion controlled.

When the release data were analyzed as per Peppa's equation, the release exponent 'n' was in the range 0.37 - 0.50 in the case of formulated matrix tablets employing HPMCK4M indicating non - Fickian (anomalous) diffusion as the release mechanism.

Table.1 Formula for Alfuzosin HCl Floating tablets containing HPMC K4M

Ingrediants(mg)	AFTA1	AFTA2	AFTA3	AFTA4	AFTA5
Alfuzosine Hcl	10	10	10	10	10
HPMC K4M	15	30	45	60	75
$NaHCo_3$	22.5	22.5	22.5	22.5	22.5
PVP K-30	3	3	3	3	3
Magnesium stearate	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5
MCC	96.5	81.5	66.5	51.5	36.5

Table.2 Physical Characterstics of Alfuzosin HCl Matrix Tablets containing HPMC K4M

Formulation	Hardness (Kg/cm^2)	Weight Variation (%)	Friability (%)	Assay Values (%)	Floating Lag Time (sec)	Floating Time (Hrs)
AFTA1	4±0.67	0.786±0.06	0.54±0.04	96.84±0.41	35	12
AFTA2	4±0.75	0.658±0.15	0.33±0.12	96.36±0.53	34	12
AFTA3	4±0.84	0.961±0.28	0.52±0.14	98.03±0.93	32	12
AFTA4	4±0.45	0.997±0.15	0.58±0.04	99.62±0.65	31	12
AFTA5	4±0.95	1.027±0.02	0.37±0.08	97.25±0.65	29	12

Table.3 *In vitro* Drug release from floating tablets containing HPMC K4M

Time (hrs)	Cumulative amount of Drug Release				
	AFTA1	AFTA2	AFTA3	AFTA4	AFTA5
0.5	101.03±0.11	25.14±0.1.21	14.32±0.32	13.52±0.29	13.19±0.74
1		33.73±0.84	21.61±0.45	19.60±0.87	18.51±0.37
2		49.56±0.36	32.73±0.42	30.52±0.65	28.54±0.34
3		62.84±1.18	41.75±0.76	37.84±0.53	35.99±0.48
4		99.29±0.97	44.86±0.94	41.13±0.87	41.98±0.73
5			50.91±0.85	45.96±0.74	44.14±0.71
6			56.51±0.37	54.85±0.32	51.09±0.95
7			61.86±0.98	74.10±1.15	60.20±1.44
8			100.58±0.64	90.34±0.46	75.84±0.74
9				101.08±0.75	85.98±0.48
10					98.04±0.42
11					98.81±0.74
12					99.15±0.74

*** Mean Percent of Alfuzosin HCl Released ($\bar{x}$ ± s.d) (n = 3)**

Table 4. Correlation coefficient (r) values in the analysis of release data as per Zero order, First order and Higuchi Equation model

Formulation	Correlation coefficient ('r' value)		
	Zero order plot	First order plot	Higuchi plot
AFTA1	0.999	0.867	0.999
AFTA2	0.978	0.829	0.961
AFTA3	0.951	0.989	0.934
AFTA4	0.972	0.848	0.937
AFTA5	0.988	0.847	0.960

Table.5 Alfuzosin HCl drug release characterstics of matrix tablets

Formulation Code	Polymer Concentration (%)	T_{50} (h)	T_{80} (h)	K_0 (mg/h)	K_1 (h^{-1})	'n' in Peppas equation
AFTA1	10	-	-	202.06	-	-
AFTA2	20	1.93	3.51	21.69	1.00	0.616
AFTA3	30	5.12	7.52	9.55	0.121	0.602
AFTA4	40	5.89	7.31	9.65	0.204	0.648
AFTA5	50	5.91	8.52	8.73	0.275	0.647

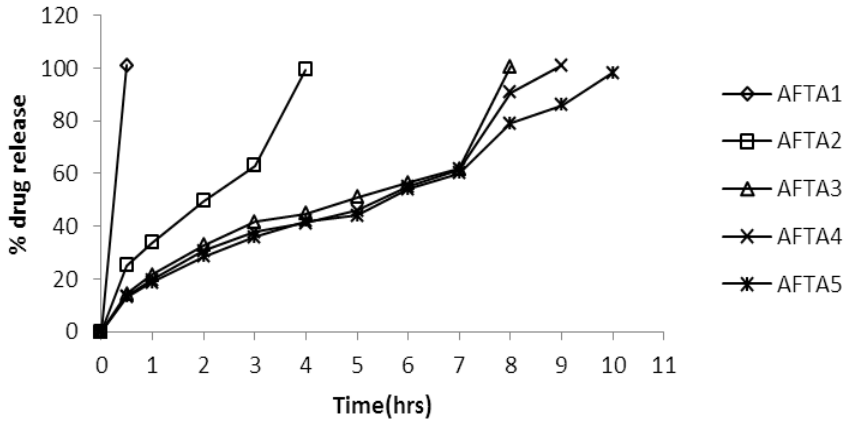

Fig .1 Percent (%) Drug Release Vs Time Curve of tablets containing HPMC K4M

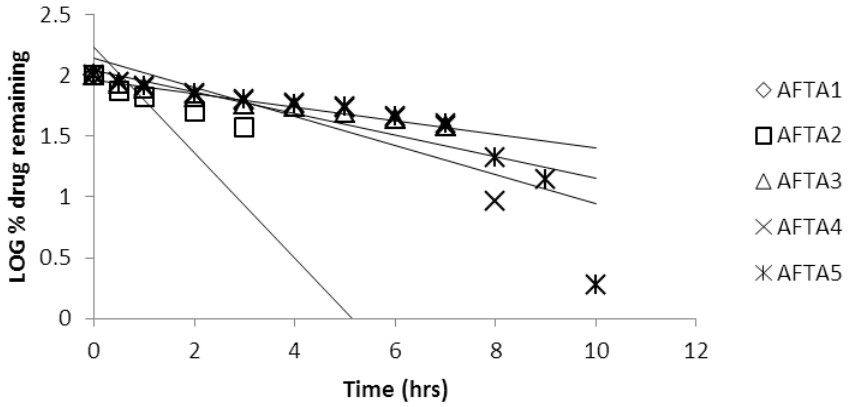

Fig .2 Log% Drug Remaining Vs Time Curve of Tablet Containing HPMC K4M

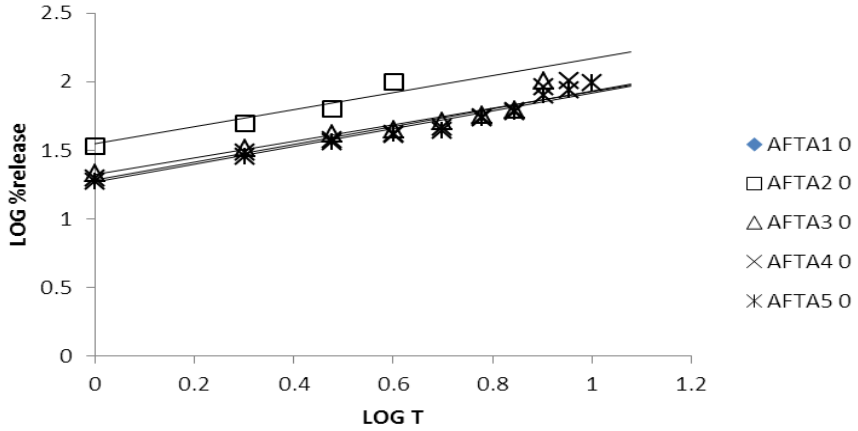

Fig . 3 Log % release Vs Log T Curve of Tablet containing HPMC K4

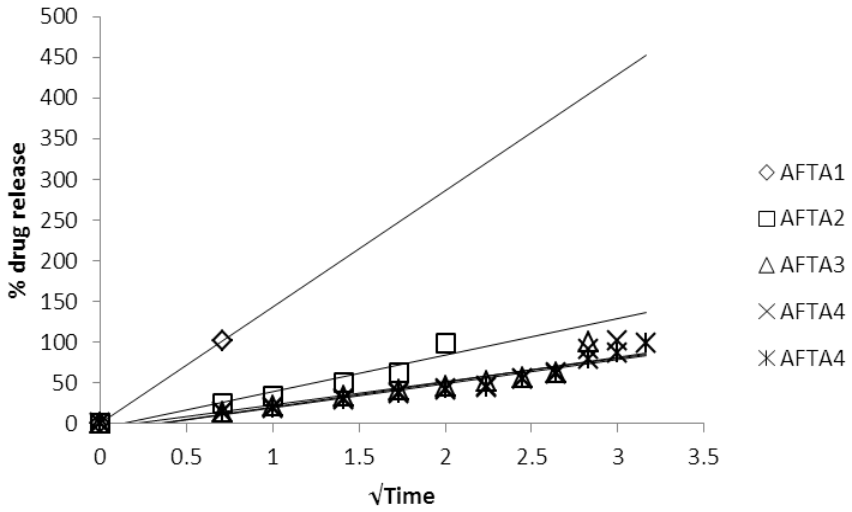

Fig.4 Percent (%) Drug Release Vs Square Root of Time Curve of Tablet containing HPMC K4M

CONCLUSIONS

1. The Hardness of the tablets was in the range of 4-6 kg/sq.cm. The weight loss in the friability test was less than 0.48 % in all the cases. All the matrix tablets prepared contained 98±2.5% of the labeled claim.
2. All the tablets were found to be non- disintegrating in acidic pH 1.2. As such, the prepared tablets were of good quality with regard to drug content, hardness and friability. As the tablets formulated were non-disintegrating in acidic and alkaline fluids, they are considered suitable for a gastro retentive drug delivery system.
3. Alfuzosine HCl floating tablets were prepared and evaluated for floating lag time, total floating time by employing different percentages of K4M.
4. It was found that drug release was controlled up to 12 hours due to low viscosity of HPMC K4M even at high concentrations also.
5. HPMC K4M was considered for floating controlled release.

REFERENCES

1. T. J. Higuchi, Pharm. Sci., 1963; 52: 1145.
2. P. L. Ritger and N. A. Peppas, J. Control. Release, 1987; 5: 37.
3. C. Narendra, M. S. Srinath, and Ganesh Babu. "Optimization of Bilayer Floating Tablet Containing Metoprolol Tartrate as a Model Drug for Gastric Retention". AAPS PharmSciTech 2006; 7(2) – 34; E1-E7.
4. V.T. Thakkar,*, P.A. Shah, T.G. Soni, M.Y. Parmar, M.C. Gohel and T.R. Gandhi "Fabrication and evaluation of levofloxacin hemihydrate floating tablet". Research in Pharmaceutical Sciences, October 2008; 3(2): 1-8.
5. Arunachalam.A*, B.Stephen Rathinaraj, Ch.Rajveer, D.kumaraswami, M.umarunnisha "Design and evaluation levofloxacin floating tablets". International Journal of Applied Biology and Pharmaceutical Technology, 2010; 260-267.
6. Anroop Nair "In Vitro Controlled Release of Alfuzosin Hydrochloride Using HPMC-Based Matrix Tablets and Its Comparison with Marketed Product". Pharmaceutical Development and Technology, 2007; 12: 621–625: