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Formulation and Evaluation of Gastro Retentive Floating Tablets of Montelukast Sodium

MD. Bala Pasha* and Rama Rao Nadenla

Chalapathi Institute of Pharmaceutical Sciences,Guntur, Andhra Pradesh, India.

* Corresponding author: MD. Bala Pasha, e-mail: pashamunna@rediffmail.com

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ABSTRACT

Montelukast sodium is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma, chronic asthma attacks and to relive symptoms of seasonal allergies. The main drawback of conventional Montelukast sodium formulation is that it undergoes hepatic first pass metabolism. Thus, it shows plasma or biological half-life 2.5 to 5.5 hrs, administered as oral tablets at high doses 2-3 times per day. Thus it is decided to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability. Totally 12 formulations were formulated by using the above drugs by using two different techniques like Effervescent floating technique and Non Effervescent floating technique. Among them Formulations F1-F12 were formulated by using Montelukast sodium as a drug, whereas the formulations F1-F6 were formulated by Effervescent floating technique and formulations F7-F12 were formulated by Non Effervescent floating technique. All the formulations were evaluated for the pre compression and post compression parameters and all the formulations shows acceptable limits. The in vitro drug release profiles of the formulations F1-F12 the maximum drug release was found in the F12 formulation containing polyox WSR(90mg) as a rate retarding polymer.

Keywords: Montelukast sodium, Polyox WSR, floating gastro retentive drug delivery system.

1. INTRODUCTION

The oral route represents the predominant and most preferable route for drug delivery unlike the majority of parenteral dosage forms it allows ease of administration by the patient and highly convenient way for substances to be introduced in to the human body. Oral drug delivery systems are divided in to immediate release and modified release systems [1]. Modified release systems have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients and patient compliance as well as reducing side effects. Oral modified release delivery systems commonly include delayed release, extended release programmed release and site specific or timed release. Oral extended release dosage forms offer the opportunity to provide constant or nearly constant drug plasma levels over an extended period of time following administration. Extended release drug delivery systems offer several advantages compared to conventional drug delivery system including avoiding drug level fluctuations by maintenance of optimum therapeutic plasma and tissue concentrations over prolonged time periods, avoiding sub therapeutic as well as toxic concentrations, thus minimizing the risk of failure of the medical treatment and undesirable side effects, reducing the administered dose and reduced frequency of administered dose while achieving comparable results, Targeting or timing of the drug action. Hence it is highly desirable to develop sustained drug delivery system releasing the drug at predetermined rates to achieve optimal plasma drug levels and/or at the site of action [2, 3].

Majority of drugs are preferentially absorbed in the upper part of the small intestine. So, Gastro retentive drug delivery systems are preferred. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with GI mucosa leading to higher bioavailability and hence therapeutic efficacy, reduced time intervals for drug administration, potentially

reduced dose size and thus improved patient compliance [4-6].

FDDS are preferred as they are economic and has improved patient compliance and they are advantageous for drugs absorbed from the stomach eg: ferrous salts and for drugs meant for local action in the stomach eg: antacids, drugs with narrow absorption window in the small intestine region eg: L-Dopa. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such circumstances also it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response [9, 10].

The present work is an attempt to develop FDDS in the form of tablets taking Montelukast Sodium as the model drug. Montelukast sodium is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma, chronic asthma attacks and to relive symptoms of seasonal allergies. The main drawback of conventional Montelukast sodium formulation is that it undergoes hepatic first pass metabolism [11]. Thus, it shows plasma or biological half-life 2.5 to 5.5 hrs, administered as oral tablets at high doses 2-3 times per day. Thus it is decided to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability. The tablets prepared by direct compression technique by using different polymer concentrations to enhance gastric retention and to increase its bioavailability and duration of action.

2. MATERIALS AND METHODS

2.1 Materials

Montelukast Sodium was procured from Aristo pharmaceuticals Ltd., Polyox WSR, Polyox WSR and HPMC K100 M, Polypropylene foam powder, were purchased from S.D. Fine Chemicals (Mumbai, INDIA), sodium bicarbonate and other excipients were procured from spectrum pharma research solutions, Hyderabad.

2.2 Preparation of floating tablets By direct compression method [12]

All ingredients were collected and weighed accurately. Drug with polymers were sifted and passed through sieve #60 and then the remaining excipients were rinsed over after pre blending all ingredients in mortar for 15minutes. The entire mixture was blended for 5minutes. Then magnesium stearate was added and blended again for 5-6 minutes, lubricated powder was compressed under 8mm punch of tablet punching machine, (Cadmach model DC16 16-Station Tablet Press). The composition of different formulations is shown in tables.

2.3 Evaluation of Formulations

2.3.1 Pre compression parameters:

It includes Angle of repose, Bulk density, Tapped density, Cars index, Hausner's ratio [13].

2.3.2 Pre compression parameters:

It includes Weight variation, Hardness, Friability, Thickness and diameter, Drug content, *In-vitro* buoyancy studies, Swelling index and *In-vitro* dissolution studies [14].

3. RESULTS AND DISCUSSION

Gastro retentive floating tablets were formulated by Montelukast Sodium by Effervescent technique (i.e., from F1-F9) and by Non effervescent technique (i.e.,F10-F18).The formulated tablets have shown the results as given below:

UV Spectra of Montelukast Sodium at 10µg/ml concentration. Wavelength of maximum absorption in 0.1N HCL solution was found to be 246nm, with UV range of Montelukast Sodium was found to be 5-30mcg/ml with a regression value of 0.999.

3.1 Compatibility studies by FT-IR:

From the compatibility studies it was concluded that the functional groups that were presented in the pure drug were present in the optimized formulation with very minute changes, from this we can concluded that the drug and excipients have no interactions.

3.2 *In vitro* floating buoyancy studies:

All the formulated tablets were evaluated for the buoyancy studies for the determination of Floating Lag Time and Total Floating Time. The formulations having higher polymer concentrations exhibits total floating time for more than 20 hours than the other formulations.

3.3 Swelling Studies:

From the swelling studies of the floating tablets it was identified that the tablets formulated by effervescent technique have higher swelling index than the Non effervescent floating tablets, among them Polyox WSR having 90mg have higher swelling index.

3.4 *IN-VITRO* DRUG RELEASE STUDIES

3.4.1 *In-vitro* drug release data of Montelukast Sodium floating tablets by effervescent technique:

From the drug release studies of the gastro retentive floating tablets of Montelukast Sodium formulated by effervescent technique the maximum amount of drug release was found in F6 formulation containing Polyox WSR (90mg) as a rate retarding polymer as it has higher efficiency for retarding the drug release in the dissolution medium, but it doesn't maintain the drug release for 24hours (Table 1).

3.4.2 *In-vitro* drug release data of Montelukast Sodium floating tablets by Non-Effervescent technique:

The in vitro drug release profiles of the formulations F7-F12 shows maximum drug release in F12 formulation containing Polyox WSR in higher concentration i.e.,90mg, formulated by using Non Effervescent floating technique.

While comparing the two different floating techniques better drug release was found in Non Effervescent floating systems as they have slow swelling capacity and can prolong the floating time, due to these reasons the Non Effervescent floating system was better than the Effervescent floating systems (Table 2).

While comparing the effervescent and Non effervescent floating techniques the maximum drug release was found in the F12 formulation when compared with F6 formulation using same polymers. The Pre-compression and post-compression parameters are given in Table 3.

The drug release kinetics of the optimized formulation (F12) of the Atorvastatin follows zero order drug release with super case transport mechanism (Figures 1 and 2).

Table 1: Composition of Montelukast sodium floating tablets by Effervescent technique:

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Montelukast sodium	10	10	10	10	10	10
HPMC K100M	30	60	90	-	-	-
POLYOX WSR	-	-	-	30	60	90
PVP K30	6	6	6	6	6	6
MCC	92	62	32	92	62	32
NAHCO3	50	50	50	50	50	50
Citric acid	5	5	5	5	5	5
Mg -stearate	3	3	3	3	3	3
Talc	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**

Table 2: Composition of Montelukast sodium floating tablets by Non - Effervescent technique:

Ingredients(mg)	F7	F8	F9	F10	F11	F12
Montelukast sodium	20	20	20	20	20	20
HPMC K100M	30	60	90	-	-	-
POLYOX WSR	-	-	-	30	60	90
PVP K30	6	6	6	6	6	6
Polypropylene foam powder	50	50	50	50	50	50
MCC	97	67	37	97	67	37
Mg -stearate	3	3	3	3	3	3
Talc	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**

Table 3: Pre-compression and post-compression parameters

Parameters	Range	Parameters	Range
Angle of repose (θ) ±SD	22.58±0.22- 26.42±0.58	**Average wt in (mg)±SD**	199.84± 0.16-200.10± 0.26
Bulk density (gm/cm)±SD	0.258±0.42-0.287±0.14	**Hardness (Kg/cm2)±SD**	5.6± 0.28- 6.2± 0.52
Tappeddensity (gm/cm) ±SD	0.308±0.22-0.338±0.64	**Diameter in (mm)±SD**	7.86± 0.10 - 8.10± 0.26
Hausnerratio (HR)±SD	1.12±0.16-1.21±0.24	**Thicknessin (mm)±SD**	2.68± 0.10- 3.12± 0.18
Carr index (C.I) ±SD	11.68±0.18- 18.43±0.13	**Friability (%)±SD**	0.08± 0.26 - 0.52± 0.42
		Drug content (%)±SD	86.22±0.44- 97.28±0.16

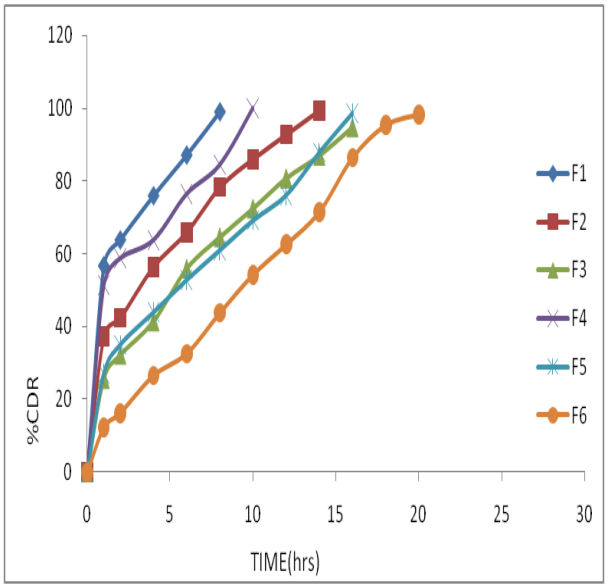

Figure 1:%CDR of F1-F6

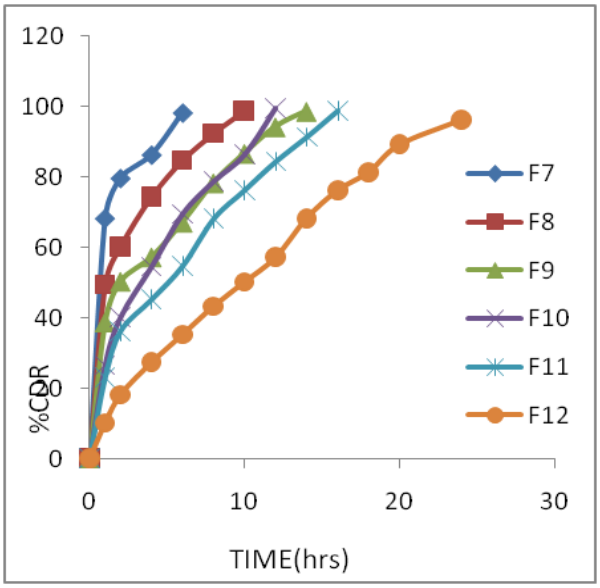

Figure 2: %CDR of F7-F12

4. CONCLUSION

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

So for increasing the gastric retention time of the some poorly acidic absorption drugs were selected for increasing the gastric retention time for increasing the bioavailability of the drug. From the results obtained it was concluded that the The in vitro drug release profiles of the formulations F1-F12 the maximum drug release was found in the F12 formulation containing Polyox WSR(90mg) as a rate retarding polymer formulated by using Non Effervescent floating technique.

5. REFERENCES

1. Chien YW. Rate controlled drug delivery systems. 2nd Ed. New York: Marcel Dekker; 2005.
2. Lescol (fluvastatin sodium) Capsules, Lescol XL (fluvastatin sodium) Extended-Release Tablets 2012 (Internet). (Cited on 22-06-13). Available URL: http://www.fda.gov/Safety /MedWatch SafetyInformation /ucm295979.htm
3. Theeuwes FG, Higuchi T. Fabrication of sustained release dosage form. U.S. patent No. 3,845,770.
4. Whitehead, L., Fell, J.T., Collett, J.H., 1996. Development of gastroretentive dosage form. Eur. J. Pharm. Sci. 4, 182-182
5. Mr. Shinde AS J Gastro retentive Drug Delivery System: An Overview., www.Pharma info.net. (Cited on 22-5-2012)
6. Amnon H, David S, Eran L, Eyal S, Eytan K, Michael F. Pharmacokinetic and pharmacodynamic aspects of gastro retentive dosage forms. International journal of pharmaceutics 2004; 277:141-153
7. Reddy LHV, Murthy RSR. Floating dosage systems in drug delivery. Crit Rev Ther Drug Carri Syst 2002; 19: 553-85.
8. Singh BN, Kim KH, Review: Floating Drug Delivery Systems: an approach to oral Controlled drug delivery via gastric retention. Journal of Controlled release 2000; 63: 235-259.
9. Shah SH, Patel NV, Stomach specific floating drug delivery system: A review. International Journal of Pharm Tech Research 2009; 1(3): 623-633.
10. Yeoe PG, Khan S, Patel VF. Floating drug delivery systems: need and development Ind J Pharm Sci 2005; 67: 265-72.
11. Drug bank (Internet). (Cited on 22-06-12). Available URL: http://www.drugbank.ca/drugs/DB01095.
12. Bhawna Khurana et.al.Formulation of time Dependent Sustained Release Tablet of Nimodipine and its Evaluation using Linear Regression Analysis . Indo American Journal of Pharm Research.2013:3(11).
13. Vezin W.R., Khan K.A. and Pang H.M., Journal of Pharmacy and Pharmacology 1983;35: 555-558
14. Costa P., Sousa L. J. M., Modelling and comparison of dissolution profiles, European Journal Pharmaceutical Sciences 2001; 13:2: 123–133.

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