Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Issue 3, 2013

Research Article

FORMULATION AND EVALUATION OF FLOATING MATRIX TABLETS OF CLARITHROMYCIN USING DIFFERENT GRADES OF HPMC

WILLIAM ARPUTHA SUNDAR*, VIJAYARAGAVAN. C AND DHARANI PUROHIT

Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Anaikuttam Sivakasi 626130, India.
Email: aswilliamas@gmail.com

Received: 19 Jan 2013, Revised and Accepted: 31 Mar 2013

ABSTRACT

Floating matrix tablets are designed to prolong the gastric residence time after oral administration, at a particular site and controlling the release of drug especially useful for achieving controlled plasma level as well as improving bioavailability. Clarithromycin is one of the best antibacterial agents against Gram negative bacteria. With this objective, floating dosage form containing Clarithromycin as drug was designed for the treatment of *Helicobacter pylori*. Tablets containing API, hydroxypropyl methyl cellulose (HPMC), and different additives were prepared by wet granulation. The study shows that tablet composition and mechanical strength have great influence on the floating properties and drug release. Incorporation of gas-generating agent together with polymer improved drug release, besides optimal floating (floating lag time <1.5min; total floating time >20 h). The drug release was sufficiently sustained (more than 12 h). The optimized formulation was obtained using 50% clarithromycin, 14.47% HPMC K15M, 3.9% HPMC K4M, which gave floating lag time < 1.5min with a total floating time > 20 h, *in vitro* release profile very near to the target *in vitro* release profile.

Keywords: Floating matrix tablets, Clarithromycin, *H.pylori*, HPMC, Dissolution

INTRODUCTION

An ideal drug delivery system (DDS) should aid in the optimization of drug therapy by delivering an appropriate amount to the intended site and at a desired rate. Hence, the DDS should deliver the drug at a rate dictated by the needs of the body over the period of treatment [1]. An oral drug delivery system providing a uniform drug delivery can only partly satisfy therapeutic and biopharmaceutical needs, as it doesn't take into account the site specific absorption rates within the gastrointestinal tract (GIT). Therefore there is a need of developing drug delivery system that releases the drug at the right time, at the specific site and with the desired rate [2].

There has been considerable research over the last decade on the possibility of controlled and site-specific delivery to the GIT by controlling the gastrointestinal transit of orally administered dosage forms using gastro retentive drug delivery system (GRDDS). Such GRDDS possess the ability of retaining the dosage forms in gastrointestinal tract (GIT) particularly, in the stomach for long period [3]. The transit time in GIT i.e., from the mouth to the anus, varies from one person to another. It also depends upon the physical properties of the object ingested and the physiological conditions of the alimentary canal**.** Several drugs are absorbed to the most extent in the upper part of the small intestine [4].

Many drugs show poor bioavailability (BA) in the presence of intestinal metabolic enzymes like cytochrome P450 (CYP3A), abundantly present in the intestinal epithelium. Their activity decreases longitudinally along the small intestine, with levels rising slightly from the duodenum to the jejunum and declining in the ileum and colon [5]**.** Clarithromycin is a macrolide antibiotic with broad spectrum of activity. It is given in the treatment of respiratory tract infections, skin and soft tissue infections [6]. Clarithromycin is used in the treatment of *Helicobacter pylori* infected disease and Lyme disease [7]. Clarithromycin is currently available in the form of tablets, which have to be, dosed twice daily. Reason for choosing clarithromycin for floating drug delivery system is that clarithromycin require to exert local therapeutic action in the stomach to kill the *H. Pylori* in the stomach, clarithromycin exhibiting site specific action in the stomach (or) upper part of the small intestine, clarithromycin is insoluble in intestinal fluids, comparatively two fold more therapeutic activity than erythromycin and also clarithromycin is used in the first line treatment [8].

Floating tablets of clarithromycin were developed to prolong Gastric residence time and to increase its bioavailability [9]. The tablets were prepared by direct compression method. Seven formulations of floating tablets of clarithromycin using the polymer of different grades namely Hydroxy Propyl Methyl Cellulose K15M (HPMC K 15 M), and Hydroxy Propyl Methyl Cellulose K4 M (HPMC K 4M) in different concentrations were prepared by wet granulation method. Sodium bicarbonate was used as a gas generating agent. Polyvinyl Pyrrolidine (PVP K30) was used as solubilizer enhancing agent.

MATERIALS AND METHODS

Clarithromycin was obtained as a gift sample from Alembic limited; Sodium bi carbonate was obtained from Panmy Speciality chemicals; HPMC K15M, HPMC K15M, HPMC K15M, Magnesium stearate, Lactose and Talc were obtained from Loba chemicals Pvt Ltd; Iso propyl alcohol and Potassium hydrogen ortho phosphate (anhydrous) were obtained from S.D.fine chemicals Pvt. Ltd.; Sodium hydroxide and Potassium chloride were obtained from Reachem laboratory chemicals Pvt. Ltd.

Seven formulations of floating tablets of clarithromycin using ingredients given in the Table No.1 Different concentrations of polymers were used to prepare floating tablets of Clarithromycin by wet granulation method. Sodium bicarbonate was used as a gas generating agent. Polyvinyl Pyrrolidine (PVP K30) is used as solubilizer enhancing agent. Lactose is used as diluent.

Table 1: Formula for the preparation of floating matrix tablets of clarithromycin

Formulation code	Clarithromycin (mg)	HPMCK_4M (mg)	HPMC k_{15}M (mg)	Lactose (mg)	Isopropyl alcohol (ml)	Sodium bi carbonate (mg)	Talc (mg)	Magnesium stearate (mg)
F_1	250	92	6	100	q. s	46	4	2
F_2	250	142	6	50	q. s	46	4	2
F_3	250	19.8	72.36	100	q. s	51.84	4	2
F_4	250	92	106	-	q. s	46	4	2
F_5	250	19.8	72.36	60	q. s	91.84	4	2
F_6	250	19.8	172.36	-	q. s	51.84	4	2
F_7	250	39.8	72.36	80	q. s	51.84	4	2

Seven formulations of Clarithromycin were prepared. Pure clarithromycin, sodium bicarbonate, HPMC K 15M and HPMC K4M with different concentrations, Polyvinyl Pyrrolidone (PVP K30), sodium bicarbonate and lactose were mixed together in a blender to get uniform mixture. The blended powder was passed through sieve no. 100. Granules were prepared using isopropyl alcohol as a solvent. Prepared granules were dried in hot air oven at 60^0C for 1 hr. After drying the granules were passed through sieve no. 22. The dried granules were subjected to different pre formulation studies namely Bulk density, Tapped Density and Angle of Repose. Finally the dried granules were lubricated with talc and magnesium stearate, uniformly mixed and then compressed into tablets by Mini press -1 compression machine.

RESULTS AND DISCUSSION

The lubricated powder blend was evaluated for density parameters like bulk density, tapped density, compressibility index and Hausner's ratio was calculated to estimate the flow properties. The compressed tablets were characterized by their physical properties. The average tablet weight was determined from 20 tablets. Tablet hardness was tested using Monsanto tablet hardness tester. Friability of the tablets was determined by Roche friabilator. Tablet friability was calculated as the percentages of weight loss of 20 tablets after 100 rotations. The physical parameters of granules were provided in Table No. 2.

Table 2: Evaluation of lubricated powder blend of clarithromycin

S. No.	Parameters	Clarithromycin granules						
		F1	F2	F3	F4	F5	F6	F7
1	Bulk density(gm/cc)	0.3135	0.3265	0.256	0.3481	0.3196	0.2307	0.247
2	Tapped density(gm/cc)	0.3605	0.3964	0.4326	0.3562	0.4621	0.3134	0.3241
3	Angle of repose(°)	34°93'	31°56'	33°05'	34°57'	34°56'	35°41'	35°00'
4	Compressibility index (%)	12.19	11.56	12.65	12.81	12.34	12.10	11.44
5	Hausner's ratio	1.21	1.31	1.21	1.21	1.31	1.21	1.20

The compressed tablets were characterized by their physical properties. The average tablet weight was determined from 20 tablets. Tablet hardness was tested using Monsanto tablet hardness tester. Friability of the tablets was determined by Roche friabilator. Tablet friability was calculated as the percentages of weight loss of 20 tablets after 100 rotations. Buoyancy lag time (minutes), the duration of Buoyancy and swelling index were also determined. The physical parameters of granules and compressed tablets were provided in Table No. 3.

Table 3: Evaluation of compressed tablets of clarithromycin

S. No.	Parameters	Clarithromycin tablets						
		F1	F2	F3	F4	F5	F6	F7
1	Hardness (kg/cm2)	4.5±0.2	4.1±0.2	4.4±0.2	4.0±0.2	4.3±0.2	4.4±0.2	4.5±0.2
2	Friability (%)	0.25	0.18	0.02	0.01	0.12	0.23	0.23
3	Uniformity of weight (mg)	499±1.5%	501±2.0%	502±1.7%	504±1.8%	496±1.4%	504±1.6%	499±1.5
4	Drug content (%)	98.83±0.50	91.86±0.3	95.58±0.2	97.91±0.3	102.9±0.2	97.2±0.2	95.86±0.2
5	Thickness (mm)	4.0±0.05	4.1±0.05	4.3±0.03	4.3±0.05	4.2±0.02	4.4±0.03	4.4±0.03
6	Buoyancy lag time (minutes)	›10	Tablets did not float	3.5	1.5	2.5	1.5	3.0
7	Duration of buoyancy (hours)	›20	-	›20	›20	›20	›20	›20
8	Swelling index	50%	55%	70%	80%	71%	85%	76%

The dissolution rate studies were performed to evaluate the dissolution characteristic of clarithromycin from floating tablets with seven formulations and to characterize and determine the optimized formulation among them. The drug release of seven formulations was compared with each other. The results are presented in Table No.4. The dissolution study of all the formulation was found to be F1-63.7%, F2-55.1%, F3-53.1%, F4-65%, F5-44.53%, F6-69.70%, F7-53.00%. From all the formulations formulation F_5 shows better delay in drug release when compared to other six formulations. The results are given graphically in fig 1.

Table 4: In vitro release study of clarithromycin

S. No.	Time of sampling (hours)	Percentage of drug release (%)						
		F_1	F_2	F_3	F_4	F_5	F_6	F_7
1	1	27.00	18.10	5.60	15.14	12.38	14.10	27.30
2	2	33.80	24.60	12.50	22.15	16.88	20.10	32.40
3	3	38.10	30.50	19.05	30.01	22.50	31.00	37.70
4	4	42.10	35.00	23.50	41.09	27.00	43.20	41.00
5	5	45.00	40.10	29.20	48.08	31.31	49.10	42.10
6	6	50.60	45.90	39.40	54.20	34.88	55.10	45.00
7	7	56.30	51.80	44.80	60.00	40.49	63.70	47.10
8	8	60.00	52.00	48.00	62.69	41.50	65.10	49.13
9	9	61.10	53.70	51.10	64.92	43.51	68.10	51.01
10	10	63.70	55.10	53.00	65.21	44.53	69.70	53.00

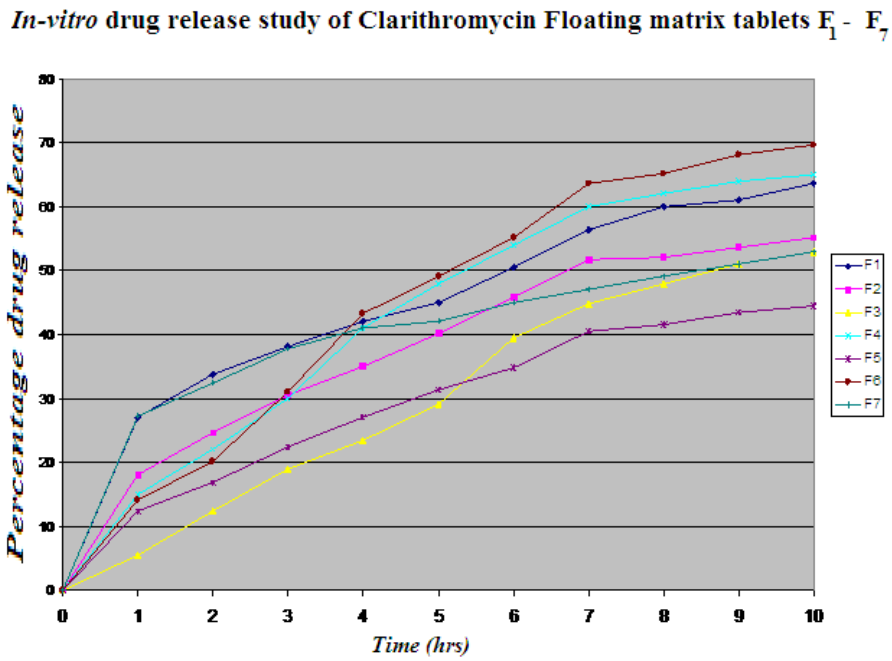

Fig 1: In-Vitro release study of Clarithromycin floating matrix tablets

CONCLUSION

Floating matrix tablets of Clarithromycin tablets by wet granulation method were prepared. Pre compression and post compression parameters were evaluated and the optimized formulation was obtained successfully. There has been a number of floating drug release system for various drugs investigated to improve the bioavailability and compliance clinical evaluation generally showed improvement in treatment with extended release dosage forms. In the present study, clarithromycin floating tablets was attempted and showed encouraging results. Therefore further refinement in the formulations can be attempted. Such an attempt will be useful to put in market for the near future.

REFERENCES

1. Khalid Khan M., Khan MF., Mustafa G and Sualah M. Bioquivalence study of two oral formulations of clarithromycin in human male subjects. Pakistan journal of pharmaceutical science. 2011. Vol. 24, No.1; 43-46.
2. Margret Chandra., Sachin., Debjit Bhowmilk., B. and Jayakar B. Formulation and evaluation of mucoadhesive oral tablet of clarithromycin. The Pharma research: 2009; 2. 30-42.
3. Sheela N., Damodharan., Shidharma Dhukar., Surekha I., and Srinivas Rao T. Formulation and evaluation of clarithromycin gastro retentive form. International journal of pharmacy and pharmaceutical science: 2010. Vol. 2, 48-55.
4. Shah SH., Patel JK., and Patel NV. Stomach specific floating drug delivery system. International Journal of Pharm Tech Research, 2010. Vol. 1(3), 623-633.
5. Sanjay Patel S., Ray S and Thakur RS. Formulation and evaluation of floating drug delivery system containing clarithromycin for *Helicobacter pylori*. Acta Poloniae Pharmaceutica ñ Drug Research, 2006. Vol. 63(1): 53-61.
6. Rajesh M., Kamarapu Nagaraju., and Seyed Mohammed Buhary. Formulation and evaluation of Clarithromycin immediate release film coated tablets. International Journal of Pharmacy and Pharmaceutical Sciences, 2012, Vol 4: 352-357.
7. Chudiwal PD., Pawar PL., Nagaras MA., Mandlik SK., and Pandya SV. Statistical Evaluation and Optimization of Influence of Viscosity and Content of Polymer on Floating Microspheres of Clarithromycin. International Journal of PharmTech Research (USA). Vol.1, No.4, 1366-1372.
8. Aphale Sanjivini., Shinde Swapnila., Dhat Shalaka., Bagul Uddhav and Saluja Jagdish. Development and evaluation of hollow microspheres of clarithromycin as a gastroretentive drug delivery system using Eudragit polymers. International Journal of Pharma and Bio Sciences. 2011. Vol. 2(3), 344-58.
9. Pradeep Nimase K and Vidyasagar G. Preparation and evaluation of floating calcium alginate beads of clarithromycin. Der Pharmacia Sinica, 2010. 1 (1), 29-35.