Available online on www.ijcpr.com (ISSN: 0976 822X)

International Journal of Current Pharmaceutical Review and Research

Volume 1, Issue 3, November 2010 - January 2011

Research Article

Formulation, Development and Evaluation of floating tablet of Metformin Hydrochloride using optimization of gas generating agent

Gaur A* and Shah H. P.

Department of Pharmaceutical Sciences, Jaipur National University,Jagatpura,Jaipur,Rajasthan,India -302025

Abstract: The present study deals with drug release enhancement of Metformin Hydrochloride using floating technology by optimization of gas generating agent to improve the buoyancy time. Metformin hydrochloride is a oral antihyperglycemic agent of biguanide class used in treatment of type 2 Diabetes. It is hydrophilic drug which absorbed slowly and not completely form the gastrointestinal tract. The absolute bioavailability is reported to be 50-60%. This technology uses direct compression method to prepare floating tablet of Metformin Hydrochloride with release retardant polymer HPMC K-100, PVP K-30, Carbopol 934p and different concentration of gas forming agents sodium bicarbonate and citric acid. The floating behavior and in vitro dissolution studies ware carried out. From the result final formulation release was found to be approximately 96% in 24 hr, while the floating lag time was observed to be 3 min and the tablet remained floatable throughout studies. Form the result of the study we conclude that incorporation of gas generating agent produced initial burst-effect due to production and release of CO_2 form polymeric matrix. Increased concentration of sodium bicarbonate results in increased bursting effect. Optimum concentration of sodium bicarbonate was found to be 8-10% to produce low floating lag time. Thus, with using of optimum concentration of gas generating agent the floating tablet of Metformin Hydrochloride was successfully developed.

Key words: Metformin hydrochloride, sodium bicarbonate, floating lag time

Corresponding author
Email: ajay_gaur11@yahoo.com

Introduction

During the last decade, many formulations have been performed concerning sustained release mechanisms of drugs. Orally administration of drug is the predominant and most accepted route for drug delivery because of several advantages like patients compliance, easy to administration etc. amongst the sustained release, the floating drug delivery system of drug is predominant method for sustained release of Metformin hydrochloride. Depending on the mechanisms of buoyancy, two different methods viz., effervescent and non-effervescent systems have been used in the development of floating drug delivery system. Effervescent methods utilize polymer metrics like HPMC K100, Carbopol 934p, and gas generating agent like sodium bicarbonate, citric acid. Proper optimization of gas generating agent is important in improvement of floating lag time.

Metformin Hcl is a biguanide antihyperglycemic agent that improves glucose tolerance in patients with type II diabetes. Metformin Hydrochloride is incompletely absorbed from gastrointestinal tract, it has absorption window confined to upper part of gastrointestinal tract .It has half life of 1.7 hours and its absolute bioavailability is reported to be about 45-50% of the administered dose, hence it is a suitable candidate for gastroretentive floating drug delivery system.

Materials and Methods

Metformin hydrochloride and HPMC K 100were received as gift sample from JCPL pharmaceuticals Pvt. Ltd., jalgaon. Sodium bicarbonate and citric acid was purchased form Merck.

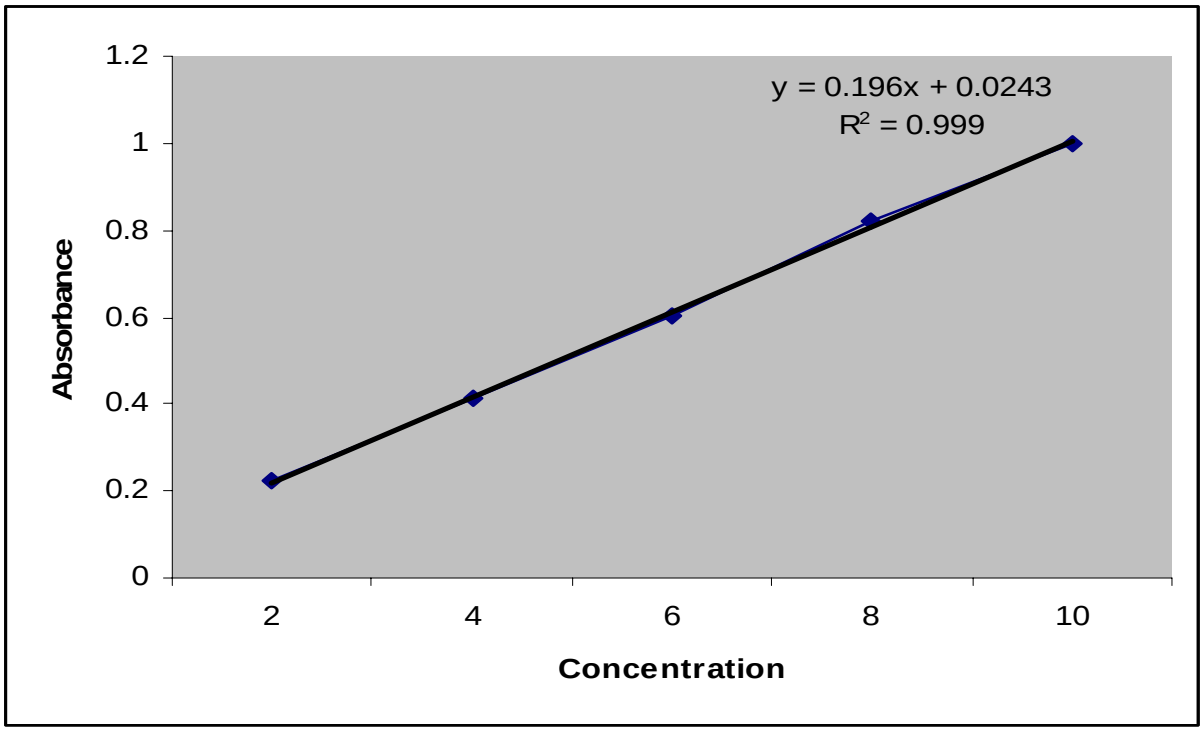
Preparation of floating tablet

1) Weigh accurately Metformin hydrochloride, HPMC K 100, PVP K 30, Carbopol 934p and talc according to formula given in table 1.
2) Then passed all above materials through different required sieve for uniformity.
3) Mix the drug with all above excipient geometrically for 10 min to achive homogeneous blend.
4) The mixed the Magnesium stearate with above homogeneous blend for 3 min.
5) Tablet ware prepared by direct compression technique using cadmach single punch machine.

Table 1: Ingredients of different Batch Numbers

Ingredients (mg per tablet)	Batch No.		
	A	B	C
Metformin hydrochloride	500	500	500
HPMC K 100M	125	125	125
PVP K-30	56	56	56
Carbopol 934p	25	25	25
Sodium bicarbonate	40	60	70
Citric acid	40	20	10
Talc	7	7	7
Magnesium stearate	7	7	7

Figure 1: Standard curve of Metformin hydrochloride at 233nm



Evaluation of tablet

(1) Floating lag time

The tablets were placed in a 100ml beaker containing 0.1 N HCL and the time required for the tablet to rise to the upper surface is noted.

(2) In-vitro dissolution study

The Metformin Hydrochloride release from different bi-layer formulation was determined using USP Type-2 apparatus under sink condition. The dissolution medium was 900ml simulated gastric fluid (pH 1.2, no enzyme) at 37± 5℃, paddle speed 50rpm to stimulate in-vivo condition. The formulation was subjected to dissolution test for 24 hr. Sample(5ml) was withdrawn at predetermined interval, filtered through whatmann filter paper and replaced by an equal volume of dissolution medium. Drug content in the dissolution sample was analyzed at 233mm by using UV spectrophotometer.

Table 2: Floating lag time of A,B,C batch

Batch	Floating lag time	Total floating time
A	4 min 33 sec	>8
B	2 min 47 sec	>12
C	2min 01 sec	>12

Table 3: Dissolution profile of A,B & C Batch

	% Concentration		
Time (Hour)	**A**	**B**	**C**
0	0	0	0
0.5	13.32	14.57	15.76
1	23.45	25.42	30.45
1.5	32.45	34.67	36.01
2	42.87	39.56	40.89
3	49.98	43.78	47.67
4	56.78	48.56	50.56
5	64.56	54.13	56.89
6	71.23	64.56	66.76
7	74.87	66.9	71.45
8	80	70.45	76.34
9	81.45	74.67	78.56
10	85.56	84.56	85.49
24	97.45	99.01	98.91

(3) Floating time

The total floating time of tablet was studied in USP type-2 dissolution apparatus a at 37± 5 ℃ in 900ml simulated gastric fluid (pH 1.2, no enzyme). The time of floatation was observed visually.

Figure 2: Floating lag time of A,B & C batch

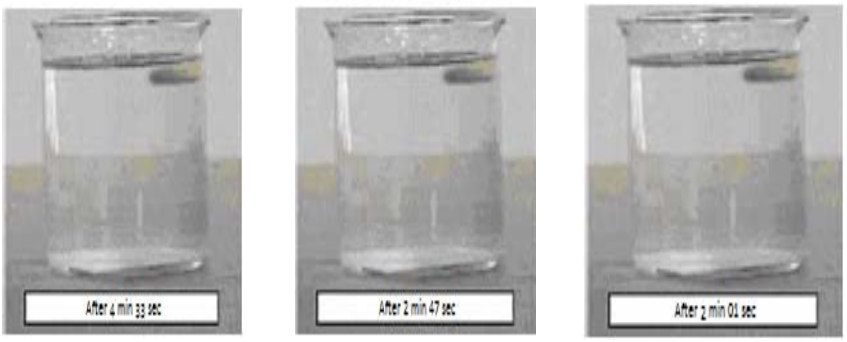
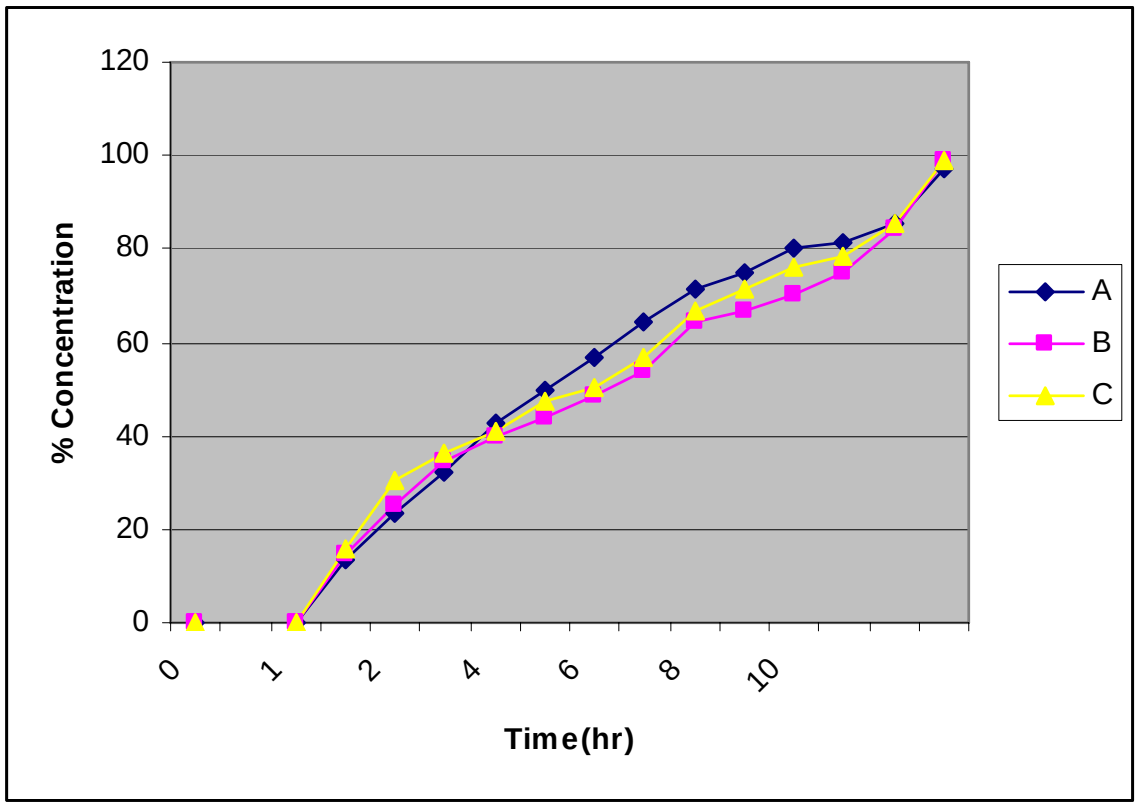


Figure 3 Dissolution profile of Different batch A, B & C



Result and Discussion

The floating tablet of Metformin Hydrochloride using optimization of different gas forming agent, Sodium bicarbonate and citric acid was prepared and evaluated for lag time, total

floating time and drug release profile to increase its bioavailability and its local action. In the present study three formulations were prepared using different concentration of sodium bicarbonate and citric acid and evaluated for lag time.

On the immersion in a 100ml beaker containing 0.1 N HCL solution the tablets were float by bursting effect of gas forming agent. Incorporation of gas generating agent produced burst-effect due to production and release of generated CO_2 from polymer matrix. Higher concentration of sodium bicarbonate results into higher bursting effect.

All formulated batches (A, B & C) passed the weight variation test, hardness test, friability and physical characteristics. Increase in hardness will decrease the porosity of the tablet and ultimately to the water penetration and floating lag time. In such cases, it would be necessary to go up to 10% sodium bicarbonate to get a low floating lag time in presence of other excipients. Formula A contains 5% sodium bicarbonate and 5% citric acid. Formula B contains 7.5% Sodium bicarbonate and 2.5% citric acid and Formula C contains 8.75 sodium bicarbonate and 1.25% citric acid. Formula A showed high floating lag time compared to formula B. Formula C showed less floating time as compared to formula B but high bursting effect than Formula A and B. Formula B is optimum for floating of tablet that showed less floating lag time and less bursting effect.

Conclusion

The floating tablet of Metformin Hydrochloride with polymer and different concentration of gas forming agent was formulated. Formula B was found to be .optimum. Thus it was conclude to use sodium bicarbonate 8-10% to get least floating.

References:

1) M.M varma et al, Formulation and Evaluation of floating drug delivery system of Metformin Hydrochloride, Journal of Chemical and pharmaceutical research, 2010, 2(2), 274-278.
2) Ziyaur rahman et al, Design and evaluation of floating tablets of captopril, Acta pharm, 56 (2006), 49-57.
3) Ravindra S Dhumal et al, Design and evaluation of bilayer floating of cefuroxime axetil bimodal release, Journal of scientific and research, vol 65, oct.2006, 812-816.
4) Timmermans, J., Moës, A.J., 1990. How well do floating dosage forms float? Int. J. Pharm. 62, 207–216.

5) Baumgartner, S., Smid-Korbar, J.,Vrecer, F., Kristl, J., 1998. Physical and technological parameters influencing floating properties of matrix tablets based on cellulose ethers. STP Pharma Sci. 8, 285–290.
6) 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.
7) K Raghuram Reddy, Srinivas Mutalik, Srinivas Reddy, Once-daily sustained release matrix tablets of Nicorandil: Formulation and in vitro evaluation, AAPS PharmSciTech; 2003,4(4): 1-9.
8) Aulton ME, Wells TI, Pharmaceutics: The Science of Dosage Form Design. London, England, Churchill Livingston; 1998;247.
9) Cooper J, Gun C, Powder Flow and Compaction. Inc Carter SJ, Eds. Tutorial Pharmacy. New Delhi, hidix CBS Publishers and Distributors; 1986:211-233.
10) Chatwal, G R., Anand S K., Instrumental Methods of Chemical Analysis (Analytical chemistry). Fifth revised and Enlarged edition, Himalaya Publishing House: 2.29-2.82, 2005.
11) Chein YW. Novel Drug Delivery Systems. 2nd ed. Vol 50. New York: Marcel Dekker. Inc. 1992.
12) Yeole PG, Khan S, Patel VF. Floating drug delivery system: need and development. Ind J Pham Sci 2005;67(3):265-71.
13) Talukder R, Fassihi R. Gasroretentive delivery system: A mini review. Drug Dev Ind Pharm 2004:30(10):1019-28.
14) Shirwaikar AA, Kumar SMR, Jacob S, Rashi W, Ravi K, Recent development in floating drug delivery system for gastric retention of drugs, an overview. Ind Drugs 2006;43(9):697-703.
15) Jain NK. Pharmaceutical product development. 1st ed. Delhi: CBS Publication and Distribution. 2006.