INTERNATIONAL RESEARCH JOURNAL OF PHARMACY **ISSN 2230 – 8407**
Available online http://www.irjponline.com
Research Article

DESIGN DEVELOPMENT AND EVALUATION OF TRIMETAZIDINE DIHYDROCHLORIDE FLOATING BILAYER M.R TABLETS

Biswajit Biswal
Asst. Professor, Dept. of Pharmaceutics, B. Pharmacy College Rampura-Kakanpur, Godhra, India

Article Received on: 12/05/11 Revised on: 20/06/11 Approved for publication: 11/07/11

* Biswajit Biswal, B. Pharmacy College Rampura-Kakanpur, Godhra, India, Email: bbiswalpharma@gmail.com

ABSTRACT
Modified release tablet are coated or uncoated tablet containing auxiliary substance or prepared by the procedure that, separately or together are design to modify the rate or place at which the active ingredient are released. Modified release (MR) DDS is an attempt to sustain drug blood concentration at relatively constant and effective level in the body by spatial placement or temporal delivery. Thus controlled release drug delivery system (CRDDS) offer various advantages viz. reduce blood level fluctuations, minimize drug accumulation, employ less total drug, improve patient compliance, and minimize local and systemic side effects.
KEYWORDS: Floating tablet, Floating bilayer tablet, Dissolution in 1.2 pH buffer.

INTRODUCTION

Floating systems, first described by Davis in 1968, have bulk density lower than that of the gastric fluid, and thus remain buoyant in stomach for a prolonged period. Floating systems can be of effervescent or noneffervescent in nature. In effervescent gas generating excipients, e.g., bicarbonate salts and acidic ingredients are used that can form CO_2 in the presence of gastric acid. Also, volatile organic solvents have been introduced into the floating chamber to generate gas at physiological temperature. In noneffervescent systems, usually high level (about 75%) of highly swellable and gel forming excipients are used. Systems based on super porous hydrogels and porous carriers are new type of noneffervescent floating drug delivery systems. Floating granules containing Florite® RE with single (primary coated granules) or double coat (secondary coated granules) of ethylcellulose. The floating properties of secondary coated granules were better than primary coated granules. Formation of polymer bridges over the Florite® RE pores and air entrapment within covered pores was suggested as reason for floating of granules i.e. the number of pores of Florite® RE covered by polymers was more in secondary coated granules than that in primary coated granules. Formulated multiparticulate and tablet gastro retentive drug delivery system using polypropylene foam powder.

Bilayer tablets contain immediate and sustained release layer. Immediate release layer delivers the initial dose, it contains superdisintegrants which increase drug release rate and start onset of action whereas sustained release layer float due to gas generating agent and releases drug at sustained manner for prolonged period .

The biphasic system is used mostly when maximum relief needs to be achieved quickly and it is followed by a sustained release phase. It also avoids repeated administration of drug. Coronary vasodilator, antihypertensive, antihistaminic, analgesic, antipyretics and antiallergenic agents are mainly used for this system. The biphasic system may contain one or two drugs for immediate release and sustained release layer.

MATERIAL AND METHODS

Trimetazidine 2HCL was obtain as a gift sample from IPCA pharmaceutical, Dicalcium phosphate from Indico remedies Pvt Ltd, Hypermellose (K-4M) from Indicame Pvt Ltd, Povidone K-30 fromIndico remedies Pvt Ltd, Magnesium stearate from Degree pharmacy rampura, Purified Talc from Degree pharmacy rampura, Colloidal Anhydrous Silica Indico remedies Pvt Ltd, IPA Degree pharmacy rampura,Carbopol 971 P from Indico remedies Pvt Ltd,Sodium starch glycolate from Indico remedies Pvt Ltd, Sodium bicarbonate and Citric acid from Indicame Pvt Ltd

Formulation of Immediate Release Tablet

Various formulation batches of Trimetazidine dihydrochloride were prepared and those formulations showing good results were used for the preparation of immediate release tablet. Trimetazidine dihydrochloride and DCP was mixed properly with disintegrant in a mortar according to compositions. The resulting mixture or blend was passed through sieve (40#). Accurately weighed 50 mg of powder blend fed manually in to each

die of 10 stations Rimek minipress-1 tablet machine and compressed by using 8 mm flat faced punch by direct compression method. Compression force was kept constant for all formulations.

Formulation of Bilayer Floating Tablet

Bilayer tablet contains two layers i.e. immediate release layer and sustained release layer of Trimetazidine dihydrochloride. Bilayer tablets were prepared by using optimized immediate and sustained release layer. Accurately weighted 50 mg of immediate release blend and 200 mg of floating sustained release blend individually. Various batches of bilayer tablets were prepared by direct compression method according to formula **.** Initially immediate release powder blend was fed manually into the die of 10 stations Rimek minipress-1 tablet machine and then compressed at low compression force to form uniform layer. Subsequently floating sustained release layer powder blend was added over that layer and completely compressed on rotary tablet punching machine by using flat faced punch 8 mm.

Steps Involved in Bilayer Tablet Preparation

1) Filling immediate release powder in to dies
2) Slightly compressed immediate release powder
3) Ejection of upper punch
4) Addition of floating sustained release powder over immediate release powder
5) Compression of both layer
6) Ejection of bilayer tablet

RESULTS AND DISCUSSION

Dissolution studies

Dissolution media: pH 1.2 HCL buffer
Apparatus : Type-1
Volume : 900 ml
Time point Hr : 1-24
RPM : 75
Temperature : 37 ± 0.5^0c

The sample withdrawn was analyzed using UV Spectrophotometer and max absorbance was taken at 231 nm. All the result are tabulated in the given below figure

REFERENCES

1. Ahuja A., Khar R., Ali J. Mucoadhesive drug delivery systems. Drug Dev Ind Pharm 1997; 23: 489-492.
2. Amartal MH. Lobo JM., Ferreira DC. Effect of hydroxyl propyl methyl cellulose and hydrogenated castor oil on naproxen release tablets. AAPS pharmscitec. 2001; 2 (2), 1-8.
3. Ali J., Arora S., Ahuja, A., Babbar, A., Sharma, R., Khar, R., Baboota, S. Formulation and development of hydrodynamically balanced system for metformin: *in vitro* and *in vivo* evaluation. Eur. J. Pharm. Biopharm2007; 67: 196-201.
4. Arora S., Ali, J., Ahuja A, Khar R., Baboota S. Floating drug delivery system: A review. AAPS Pharm Sci. Tech. 2005; 6, E372- E390.
5. Bansal A., Chawla G., Gupta P., Koradia V. Gastroretention a means to address regional variability in intestinal drug absorption. Pharmaceutical technology2003; 7: 50-68.
6. Basak SC., Reddy J., Lucas Mani KP. Formulation and release behaviour of sustained release ambroxol hydrochloride HPMC matrix tablet. Indian J. Pharm. Sci. 2006; (09-10): 594-598.
7. Baumgartner S., Kristl J., Vrecer F., Vodopiec P., Zorko B. Optimization of floating matrix tablets and evaluation of their gastric residence time. Int. J. Pharm 2000; 195: 125-135.
8. Bussemera T., Peppasb N., Bodmeiera R. Evaluation of the swelling, hydration and rupturing pulsatile drug delivery system. Eur. J. Pharm. Biopharm 2006;56: 261-270.
9. Chaudhari P., Chaudhari S., Kolhe S., Dave, K., More, D. Formulation and evaluation of fast dissolving tablets of famotidine. Indian drugs 2005; 42 (10): 641-648.
10. Chavanpatil M., Jain, P., Chaudhari S., Shear R., Vavia P. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. Int. J. Pharm 2006; 316: 89-92.
11. Chien Y., Novel Drug Delivery Systems. 2nd ed., New York: Marcel Dekker. Inc. 1992; 1-139.
12. Garg S, Sharma S 2003. Gastroretentive drug delivery systems. Business Brief Pharmatech 5th edi, Available at: http://www. touchbriefings.com/cdps/cditem.cfm?NID-17&CID-5 Accessed: August 21, 2007.
13. Hoffman A., Stepensky D., Lavy E., Eyal S., Klausner E., Friedman M. Pharmacokinetics and pharmacodynamic aspects of gastroretentive dosages forms. Int. J. Pharm 2004; 277:141-153.
14. Jain G., Goswami J. Studies on formulation and evaluation of new superdisintegrants for dispersible tablets. International journal of pharmaceutical excipient 2005; *37*-43.
15. Karande A., Dhoke S., Yeole P. Formulation and evaluation of bilayer tablet with antihypertensive drugs having different release pattern. Indian drugs 2005; 43 (1):44-50.

Table 1: Compositions of immediate release table

Ingredients	Formulation code (Quantity in mg)	
	A1	A2
Trimetazidine dihydrochloride	10	10
Sodium starch glycolate	4.6	----
Crospovidone	----	4.6
Dicalcium phosphate	35.4	35.4
Total weight (mg)	**50**	**50**

Table 2: Formulation of Floating Modified Release Tablet

Ingredients	Formulation code (Quantity in mg)			
	B1	B2	B3	B4
Trimetazidine Dihydrochloride	50.45	50.45	50.45	50.45
Dicalcium Phosphate	44.05	40.3	44.05	45.3
HPMC K15 M	35	40	----	----
HPMC K100 M	---	---	35	40
Carbopol 971 P	30	30	30	30
Sodium bicarbonate	20	20	20	20
Citric acid	4	4	4	4
Crosspovidone	13.5	12.25	13.5	12.25
Talc	1.5	1.5	1.5	1.5
Magnesium stearate	1.5	1.5	1.5	1.5
Total weight (mg)	**200**	**200**	**200**	**200**

Table 3a: Formulation of Bilayer Floating Tablet

Ingredients	Formulation code (Quantity in mg)					
	AB1	AB2	AB3	AB4	AB5	AB6
Trimetazidine Dihydrochloride	10	10	10	10	10	10
Sodium starch glycolate	4.6	4.6	---	4.6	---	4.6
Crosspovidone	---	---	4.6	---	4.6	---
Dicalcium phosphate	35.4	35.4	35.4	35.4	35.4	35.4
TrimetazidineDihydrochloride	50.45	50.45	50.45	50.45	50.45	50.45
Dicalcium phosphate	57.05	42.75	42.75	39.0	39.0	42.75
HPMC K15 M	35	35	35	40	40	---
HPMC K100M	---	---	---	---	---	35
Carbopol 971 P	30	30	30	30	30	30
Sodium bicarbonate	20	20	20	20	20	20
Citric acid	4	4	4	4	4	4
Crosspovidone	---	13.5	13.5	12.25	12.25	13.5
Talc	1.75	2.15	2.15	2.15	2.15	2.15
Magnesium stearate	1.75	2.15	2.15	2.15	2.15	2.15
Total weight (mg)	**250**	**250**	**250**	**250**	**250**	**250**

Table 3b: Formulation of Bilayer Floating Tablet

Ingredients	Formulation code (Quantity in mg)				
	AB7	AB8	AB9	AB10	AB11
TrimetazidineDihydrochloride	10	10	10	10	10
Sodium starch glycolate	--	4.6	--	4.6	---
Crosspovidone	4.6	---	4.6	--	4.6
Dicalcium phosphate	35.4	35.4	35.4	35.4	35.4
TrimetazidineDihydrochloride	50.45	50.45	50.45	50.45	50.45
Dicalcium phosphate	42.75	39.0	39.0	33.0	18.0
HPMC K15	---	---	---	40	40
HPMC K100	35	40	40	----	---
Carbopol 971 P	30	30	30	30	30
Sodium bicarbonate	20	20	20	30	45
Citric acid	4	4	4	----	----
Crosspovidone	13.5	12.25	12.25	12.25	12.25
Talc	2.15	2.15	2.15	2.15	2.15
Magnesium stearate	2.15	2.15	2.15	2.15	2.15
Total weight (mg)	**250**	**250**	**250**	**250**	**250**

Table 4: Evaluation parameters of immediate release tablet

Evaluation Parameters	Formulation Code	
	A1	A2
Hardness (N)	64-69	61-65
Friability (%)	0.317	0.402
Disintegration time (s)	42	38
Drug content (%)	99.84	99.75
% drug release	98.00	98.75
Weight variation (mg)	47-52	48-52
Wetting study (s)	6.3-6.5	6.3-6.7
Thickness (mm)	2.2-2.43	2.23-2.71

Table 5: Dissolution data of immediate release tablet

Time (min)	A1	A2
0	0	0
3	93.2	92.9
6	98.7	96.65
9	99.9	98.23
12	99.3	99.61
15	99.5	99.75
18	97.6	101.3
21	98.9	98.3
24	97.3	98.9
27	97.6	97.0
30	98.3	98.75

Table 6: Evaluation parameters of floating Modified Release tablet

Evaluation Parameters	Formulation code			
	B1	B2	B3	B4
Hardness (N)	94-103	95-107	91-97	94-102
Friability (%)	0.412	0.361	0.497	0.504
Drug content (%)	99.10	98.89	99.56	99.20
% drug release	99.92	97.80	97.66	98.19
Weight variation (mg)	200	200	200	200
Thickness (mm)	3.57	3.56	3.56	3.58
Floating lag time (sec)	17	20	16	19
Total floating time(hrs)	>24	>24	>24	>24

Table7: Dissolution data of Trimetazidine Dihydrochloride floating tablets in 1.2 pH buffer

Time (hrs)	B1	B2	B3	B4
0	0	0	0	0
1	20.79	30.22	27	41
2	40.6	47.93	59.52	52.91
4	56.17	53.45	66.66	64.21
6	64.81	57.59	73.78	70.01
8	72.17	62.24	78.65	74.87
10	76.32	68.99	83.99	76.08
12	81.21	72.92	86.86	80.81
14	86.56	74.99	89.72	84.66
16	90.21	80.95	91.83	87.4
18	94.75	85.85	93.83	91.13
20	97.65	92.42	94.97	93.88
24	99.92	97.80	97.66	98.19

Table 8: Evaluation parameters of bilayer floating tablet

Formulation Code	Drug content (%)	Percent drug release	Weight variation(mg)	Thickness (mm)
AB1	99.02	91.43	243-255	4.16-4.21
AB2	98.20	99.46	246-254	4.19-4.26
AB3	99.12	99.87	244-253	4.21-4.27
AB4	98.22	99.36	246-255	4.19-4.29
AB5	98.55	98.29	245-253	4.21-4.29
AB6	101.03	98.84	249-256	4.22-4.32
AB7	98.55	98.53	248-258	4.20-4.29
AB8	98.65	97.76	247-255	4.24-4.29
AB9	99.32	99.69	249-257	4.27-4.37
AB10	98.65	96.59	248-256	4.24-4.33
AB11	98.77	93.28	249-258	4.26-4.30

Table 9: Evaluation parameters of bilayer floating tablet

Formulation code	Hardness (N)	Friability (%)	DisintegrationTime (sec)	Floating lagtime (sec)	Total floating time(hrs)
AB1	101-104	0.412	17	13	>24
AB2	101-104	0.505	19	16	>24
AB3	101-104	0.503	20	15	>24
AB4	98-101	0.704	16	13	>24
AB5	101-104	0.525	18	15	>24
AB6	100-102	0.617	17	18	>24
AB7	101-104	0.463	19	14	>24
AB8	101-104	0.515	20	16	>24
AB9	91-98	0.717	18	14	>24
AB10	101-104	0.429	16	17	>24
AB11	101-104	0.515	19	19	>24

Table 10a: Dissolution data of bilayer floating Modified Release tablet in 1.2 pH buffer

Time(Hr)	B.No AB1	B.No AB2	B.No AB3	B.No AB4	B.No AB5
0	0	0	0	0	0
1	31.83%	33.72%	34.77%	30.39%	29.02%
2	37.56%	39.67%	41.71%	38.81%	35.71%
4	42.75%	47.31%	49.07%	47.84%	41.18%
6	46.90%	55.71%	55.42%	54.67%	47.56%
8	51.54%	60.83%	59.85%	61.85%	53.94%
10	55.02%	64.43%	65.36%	68.81%	59.13%
12	60.33%	72.20%	70.07%	74.84%	65.33%
14	64.94%	77.04%	73.33%	80.27%	70.35%
16	69.06%	81.43%	80.01%	86.43%	77.96%
18	73.21%	87.27%	86.45%	91.81%	83.22%
20	76.90%	91.03%	91.69%	95.89%	89.16%
22	81.55%	93.67%	95.89%	98.32%	95.14%
24	85.43%	99.46%	99.87%	99.36%	98.29%

Table 10b: Dissolution data of bilayer floating Modified Release tablet in 1.2 pH buffer

Time(Hr)	B.No AB6	B.No AB7	B.No AB8	B.No AB9	B.No AB10	B.No AB11
0	0	0	0	0	0	0
1	35.38%	35.71%	34.38%	31.39%	33.03%	31.66%
2	41.18%	40.41%	42.80%	38.71%	40.13%	40.05%
4	47.11%	45.91%	48.43%	44.11%	45.45%	49.93%
6	53.92%	52.64%	55.14%	50.60%	51.52%	55.89%
8	60.08%	58.25%	62.04%	58.07%	59.21%	61.65%
10	67.99%	67.98%	68.48%	65.50%	66.10%	67.38%
12	72.05%	74.59%	73.13%	71.35%	72.05%	69.70%
14	78.39%	79.64%	78.34%	77.60%	77.12%	74.10%
16	82.65%	84.91%	82.16%	81.67%	82.17%	78.91%
18	86.37%	89.86%	85.35%	86.89%	87.42%	83.37%
20	90.10%	93.23%	90.14%	91.81%	91.46%	87.32%
22	95.05%	96.64%	94.46%	95.54%	94.29%	90.77%
24	98.84%	98.53%	97.76%	99.69%	96.59%	94.28%

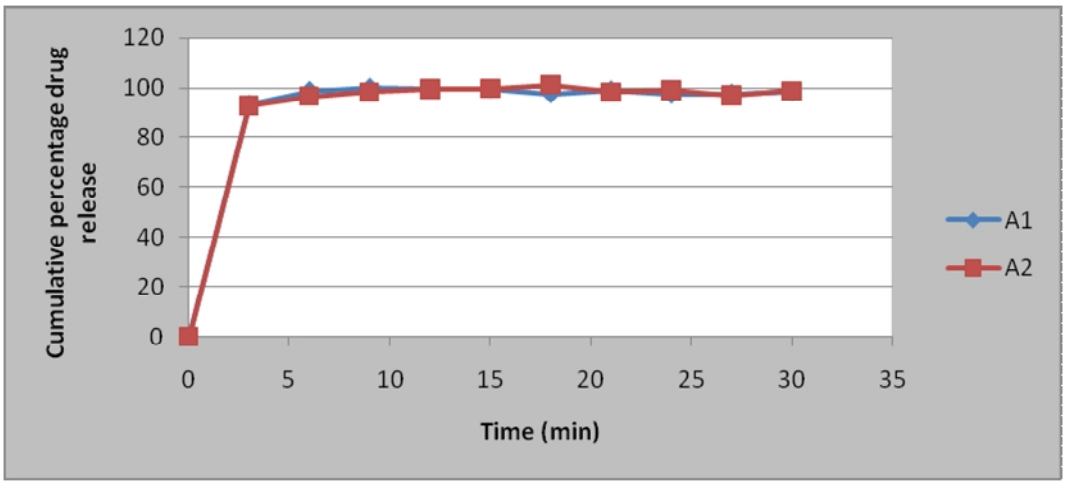

Fig.1. Dissolution profile of immediate release tablet in 1.2 pH buffer

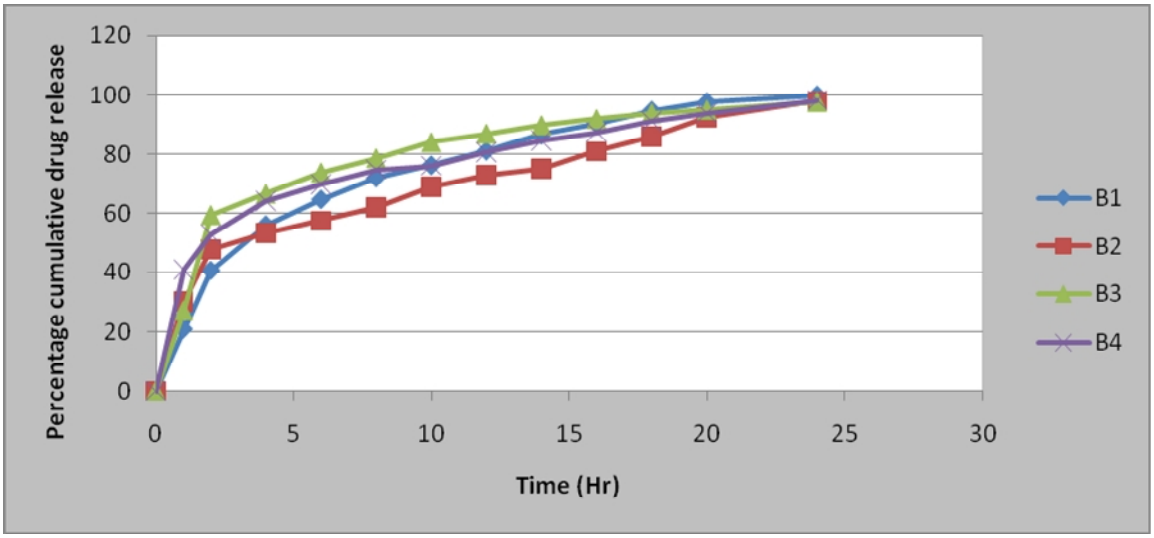

Fig.2. Comparative dissolution floating Modified Release tablets in 1.2 pH buffer (simulated gastric fluid without enzyme)

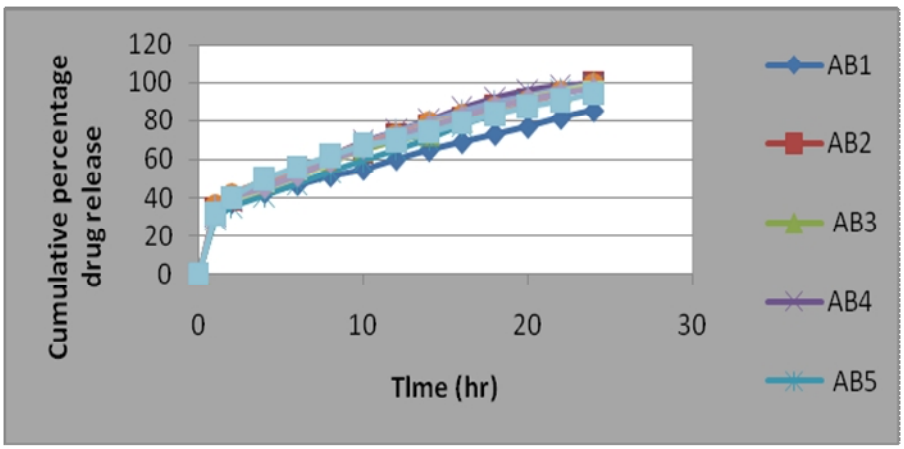

Fig.3. Comparative dissolution of bilayer floating tablets of all AB1 to AB11 batches in 1.2 pH dissolution media (simulated gastric fluid without enzyme)

Source of support: Nil, Conflict of interest: None Declared