Research Article

ISSN: 2230-7346

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

DESIGN AND DEVELOPMENT OF FLOATING TABLETS OF VALSARTAN BY USING SEED MUCILAGE OF *OCIMUM BACILICUM LINN*

S. Prasanthi[1]
M.Vidyavathi *[2]

Department of Pharmaceutics, Annamacharya College Of Pharmacy, New Boyanapalli, Rajampet-516126, A.P, India

[2] Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupathi.A.P

ABSTRACT

Gastro retentive drug delivery system is an approach to prolong the gastric residence time, there by targeting site specific drug release in the upper gastro intestinal tract for local and systemic effect. Floating tablets for Valsartan were successfully prepared using mucilage extract of *ocimum bacilicum linn* seeds. The prepared tablets were evaluated for Weight Variation, Thickness, Hardness, Friability, Drug content, Swelling studies,*Invitro* buoyancy studies and *In vitro* drug release and stability studies. Among all the formulations prepared the formulation F6 with 45mg of mucilage of *Ocimum* showed 99.5% drug release at 12hr. Stability studies of F-6 formulation have revealed that there are no significant changes during the study period.

Key Words: Valsartan, HPMC, *Ocimum bacilicum Linn*, *In vitro* drug release studies, Stability Studies.

INTRODUCTION:

Oral administration is the most convenient and preferred means of any delivery to the systemic circulation. Oral controlled release drug delivery has recently been of increasing interest in Pharmaceutical field to achieve improved therapeutic advantages such as ease of dose administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastro intestinal tract (GIT) and have short half life are eliminated quickly from systemic circulation. Frequent dosing of these drugs is required to achieve therapeutic activity. To avoid these limitations, the development of oral sustained release formulation is an attempt to release the drug slowly into the gastrointestinal tract and maintain an effective drug concentration in the systemic circulation for long time. Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site specific drug release in the upper gastro intestinal tract for local and systemic effect.[1]

Address for correspondence

M.Vidyavathi*
Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupathi.A.PIndia.
E-mail:vidvasur@rediffmail.com

Plant products serve as an alternative to synthetic products because of local accessibility, eco-friendly nature and lower prices compared to synthetic products. Natural gums and mucilages have been widely explored as pharmaceutical excipients. Thus the aim of this study was to evaluate mucilage of *ocimum bacilicum linn* as pharmaceutical excipient by formulating stomach specific drug delivery system of valsartan.[2]

Hypertension (HTN) or arterial hypertension is a chronic medical condition in which the blood pressure in the arteries is elevated. This requires the heart to work harder than normal to circulate blood through the blood vessels. Blood pressure involves two measurements, systolic and diastolic, which depends on whether the heart muscle is contracting (systole) or relaxed (diastole) between beats. Normal blood pressure is at or below 120/80 mmHg. High blood pressure is said to be present if it is persistently at or above 140/90 mmHg.[3] Valsartan belongs to the family of angiotensin II type1 receptor (AT1) antagonists and possess about 20,000 fold greater affinities for it than for the angiotensin II type 2 receptor (AT2). This action exert effects on blood pressure (BP) reduction, as well as decreases vascular smooth muscle contraction, inhibits sympathetic outflow, improves renal function and also leads to

reduction in progression of atherosclerosis lesions. The aim of the present study is to prepare gastro retentive tablets of valsartan which is a non-peptide, selective angiotension type II (AT II) receptor antagonist and used in the treatment of hypertension.

MATERIALS AND METHODS:

Valsartan was obtained as a gift sample from Aurabindo Pharma pvt.ltd, Hyderabad. *Ocimum basilicum* purchased from local market.

Mucilage was extracted from seeds of *ocimum bacilicum linn* by soaking seeds in distilled water (for about 12hrs) then blending and finally precipitated with acetone. [4,5,6]

preparation of floating tablets of valsartan using ocimum bacilicum linn.seed mucilage: [7]

Preparation of Valsartan tablets were prepared by wet granulation method by using the compositions as given in table 1.

Step1: Weighing

All the ingredients were weighed accurately as per the manufacturing formula.

Step 2: Pre sieving & mixing

Valsartan, *Ocimum* seed mucilage and HPMC were passed through #40 mesh sieve and collected in a poly bag. Above sifted materials were loaded in a planetary mixer and mixed for 15min at slow speed.

Step 3: Binder preparation

0.5gm of Starch was added in 55ml of purified water and heated until it is dissolved.

Step 4: Wet Granulation

The above prepared binder solution was added to the contents of planetary mixer and obtained the wet dough mass.Then passed through sieve to get wet granules.

Step 5: Drying

Wet granules were dried at 50ºC-55ºC by using tray drier, till desired LOD is achieved.

Step 6: Sieving milling

Dried granules were passed through #16 mesh sieve and over sized granules passed through 2.0mm multi mill at medium speed in forward direction.Finally milled granules were passed through #16 mesh sieve and loaded in a double cone blender.

Step 7: Blending

Magnesium stearate was passed through #40 mesh and it was added to the contents of double cone blender and mixed for 10 min.

Step 8: Compression

Blended material was loaded in a hopper and compressed into tablets by using (Cad mach) compression machine with (9mm) standard flat punches.

PREFORMULATION EVALUATION: [8]

The following characterization studies were carried out for 6 different formulations of Granules.(Table 1).

Angle of repose:

Angle of repose was measured according to fixed funnel standing method. Granules were weighed passed through the funnel, which was kept at a height 'h' from horizontal surface. The passed granules formed a pile of the height 'h' above the horizontal surface and the pile was measured and the angle of repose was determined for all the formulations using the formula (n=3).

$$\text{Angle of repose } (\theta) = \tan^{-1} (h / r)$$

Whereas,

'h' is the height of pile and 'r' is the radius.

Bulk density and Tapped density:

Bulk density and Tapped density were measured by using 10ml graduated cylinder. The sample poured in the cylinder was tapped mechanically for 100 times, then tapped volume was noted and bulk density and tapped density were calculated. Each experiment was performed in triplicate.

$$\text{Bulk density} = \text{Mass of powder} / \text{Bulk volume}$$

$$\text{Tapped density} = \text{Mass of powder} / \text{Tapped volume}$$

Carr's index and Hausner's ratio:

Compressibility index and Hausner's ratio were determined according to following equations.

$$\text{Carr's index (\%)} = (\text{Tapped density} - \text{Bulk density} / \text{Tapped density}) \times 100$$

$$\text{Hausner's index} = \text{Tapped density} / \text{Bulk density}$$

EVALUATION OF TABLETS: [8]

The tablets were evaluated for Appearance, Weight variation, Thickness, Diameter, Hardness and Friability to meet the Pharmacopoeial standards(Table 3).

Weight Variation:

Ten tablets were selected at random from each batch and were weighed accurately and average weights were calculated. Then the deviations of individual weights from the average weight and the standard deviation were calculated by using the formula,

$$\text{Percentage deviation} = (X - X^*/X) \times 100$$

Where as,

X → Actual weight of the tablet

X*→ Average weight of the tablet

Limit for weight variation is ± 10%

Thickness:

Thickness of ten randomly selected tablets from each batch was measured with a Slide Calipers. Then the average diameter and thickness were calculated in triplicate.

Hardness:

Hardness was determined by using Monsanto Hardness Tester in triplicate for each batch.

Friability:

Ten tablets were sampled randomly from each batch and the friability was determined using Roche type Friabilator. A pre-weighed tablet sample was placed in Friabilator which was then operated for 100 revolutions (25 rpm). The tablets were then dusted and reweighed. Then percentage friability was calculated by using the formula, **Friability index = (I - F/I) x 100**

Whereas, I→ Initial weight and F→ Final weight

Limit not more than 1%

Drug content

Three tablets were selected randomly from each batch and taken separately into three 100 ml volumetric flasks. In each flask 100 ml of 0.1 N HCl was poured and kept for 24 hrs. After filtering the solutions, the absorbance of the filtrate was measured at 251 nm.Then % drug content was determined using standard graph.

Swelling studies [9]:

Prepared tablets were weighed individually (designated as W_1) and placed separately in petri dishes containing 0.1 N HCl. At regular intervals (1, 2, 3, 4, 5 and 6hr), the tablets were removed from the Petri dishes and excess surface water was removed carefully by using the filter paper. The swollen tablets were then reweighed (designated as W_2**)**. This experiment was performed in triplicate. The swelling index (water uptake) calculated according to the following Equation**.**

Swelling index = $W_2 - W_1/W_1 \times 100$

Where, W_1 = Initial weight of tablet

W_2 =weight of Swollen tablet.

Results were tabulated and represented graphically(fig 1,table 4).

IN-VITRO DRUG RELEASE STUDIES [10, 11]

Dissolution Parameters:

Wave length	**:** 251nm
Volume	: 900 ml,0.1N HCl
Apparatus	: USP Type-II (Paddle)
RPM	: 50 RPM
Temperature	: 37.0 ± 0.5°C

In vitro dissolution studies were conducted using USP type-II dissolution test apparatus. One tablet is transferred into each dissolution flask and operated the dissolution apparatus as per dissolution parameters. Sample solutions were withdrawn at regular sampling time intervals. Replaced the aliquots withdrawn for analysis with equal volumes of fresh dissolution medium which was maintained at 37 ± 0.5°C.Then % drug dissolved were calculated by measuring absorbance at 251 nm using UV Spectrometer for each sample using standard graph.

Stability studies:

The stability studies were carried out according to ICH guidelines for best formulation. The tablets were packed in blister packing. Then tablets were stored under at Accelerated stability conditions (40±2°C/75±5% RH) and the tablets were withdrawn at every one month and the tablet parameters like description, assay and dissolution,% drug content were determined and results shown (table 5, fig 3).

RESULTS AND DISCUSSION:

In the present study different floating tablets of valsartan were prepared with and with out HPMC and *ocimum basilicum* mucilage as release retarding agent in floating tablets at three different concentrations(15mg,30 mg,45 mg). The flow properties and other derived properties were evaluated for all the 6 formulations. All the tablets proved to be within limits showing good flow properties (Table 2).

The results of physico-chemical characterizations are shown in Table 2. The thickness of floating tablets was in the range of 2.51 to 2.60 mm. The weight of the tablets

for different formulations was found to be between 198 to 202 mg with low standard deviation values, indicating uniformity of weight. The hardness for different formulations was found to be between 4.93 to 5.89 kg/cm^2 indicating satisfactory mechanical strength. The friability was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet(table 3).

The tablets were also evaluated for *Invitro* buoyancy property and floating tablets containing HPMC exhibited buoyancy lag time of 2 to 4 mins., & floated for 24hrs, while the floating tablets containing *ocimum basilicum* mucilage exhibited same buoyancy lag time of 2 to 4 mins and floated for 24 hrs., as per the results shown in Table 4. Swelling index of all tablets is within the range of 40 to 200 and F4 has shown highest swelling index. *Invitro* dissolution studies were carried out in 0.1 N HCl. The study was performed for 12 hrs and cumulative drug release was calculated. F6 formulation which has 45 mg of mucilage showed drug release of above 99% & the results were represented graphically in figure 2.The stability study results are shown in Table 6 and Figure 3. The tablets have showed the same results after first month as that of initial results at all conditions. After second month and third month the tablets have showed the same results as that of initial results at accelerated stability condition with a slight variation (±2% and ±4%) in assay was observed. .

CONCLUSION:

Floating tablets for Valsartan were successfully prepared using mucilage of natural polymer *ocimum baisilicum* by wet granulation technique. The prepared tablets were evaluated for Weight Variation, Thickness, Hardness, Friability, Drug content, Swelling studies *Invitro* drug release,

Invitro buoyancy and stability studies. Among all the tablets prepared the tablet with 45mg of *Ocimum* has showed the dug release of 99.5% at 12 hr and floated for more than 24 hrs (fig 6) . Stability studies have revealed that there are no significant changes during the study period. It is concluded that the mucilage of *ocimum baisilicum* can be safely , cheaply used as floating polymer and release retarding material as comparable to HPMC a popular semisynthetic polymer in the development of controlled release drug delivery systems.

ACKNOWLEDGEMENTS

The author is thankful for the cooperation and facilities provided by the institute with kind permission of Sri C. Gangi Reddy, Chairman, AITS and Prof. C.Gopinath, Principal, Annamacharya college of pharmacy. The author is also grateful to the Auribindo Pharma, Hyderabad for providing free drug sample of valsartan.

Table 1: Formulation of valsartan floating tablets

S.No.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Valsartan	80	80	80	80	80	80
2.	HPMC	15	30	45	-	-	-
3.	*Ocimum basilicum* mucilage	-	-	-	15	30	45
4.	Sodium bicarbonate	15	15	15	15	15	15
5.	Lactose	84	69	54	84	69	54
6.	Magnesium stearate	3	3	3	3	3	3
7.	Talc	3	3	3	3	3	3
	Total weight(mg)	200	200	200	200	200	200

Table 2: Micromeritic properties of granules

Formulation code	Angle of Repose (Mean±SD)	Bulk density (Mean±SD)	Tapped density (Mean±SD)	Carr's Index (Mean±SD)	Hausner's Ratio (Mean±SD)
F1	29.9±0.25	0.424±0.03	0.487±0.012	12.93±1.82	1.141±0.05
F2	30.1±0.32	0.436±0.018	0.507±0.01	11.03±1.74	1.162±0.07
F3	30.7±0.64	0.471±0.021	0.524±0.01	12.11±1.61	1.111±0.03
F4	28.7±0.91	0.454±0.018	0.536±0.015	13.29±2.12	1.183±0.01
F5	29.1±0.69	0.412±0.011	0.492±0.02	12.52±2.32	1.16±0.03
F6	28.5±0.52	0.425±0.026	0.485±0.09	12.03±2.01	1.23±0.09

Table 3: Physicochemical parameters of tablets

Formulation code	Weight Variation(mg) (Mean±S.D)	Thickness (mm) (Mean±S.D)	Hardness Kg/cm^2 (Mean±S.D)	Friability (%) (Mean±S.D)	Drug content (%) (Mean±S.D)
F1	198 ± 0.13	2.60 ± 0.03	4.93 ± 0.11	0.67 ± 0.04	99.47±0.36
F2	199 ± 0.45	2.53 ± 0.31	5.81 ± 0.07	0.92 ± 0.02	98.49±0.61
F3	198 ± 0.16	2.59 ± 0.23	4.97 ± 0.14	0.87 ± 0.05	98.03±0.15
F4	200 ± 0.21	2.50 ± 0.08	5.01± 0.16	0.69 ± 0.01	99.53±0.99
F5	202 ± 0.17	2.52 ± 0.16	5.83 ± 0.04	0.59 ± 0.03	99.26±0.30
F6	201 ± 0.32	2.51 ± 0.12	5.89 ± 0.02	0.61 ± 0.04	98.50±0.45

Table 4: Swelling studies of F1 to F6 formulations.

Time (hrs)	Swelling index profile of all formulations					
	F 1	**F 2**	**F 3**	**F 4**	**F 5**	**F 6**
1	41.42	38.42	49.28	45.49	36.48	50.24
2	84.14	74.84	82.4	92.64	63.74	83.48
3	167.49	147.43	179.48	189.49	139.63	165.67
4	182.43	168.47	209.37	231.64	158.72	182.43
5	197.54	182.43	224.64	247.38	174.32	196.54
6	218.68	198.49	239.48	261.48	192.38	214.67

Figure 1: Swelling Index Data For Formulation F1-F6

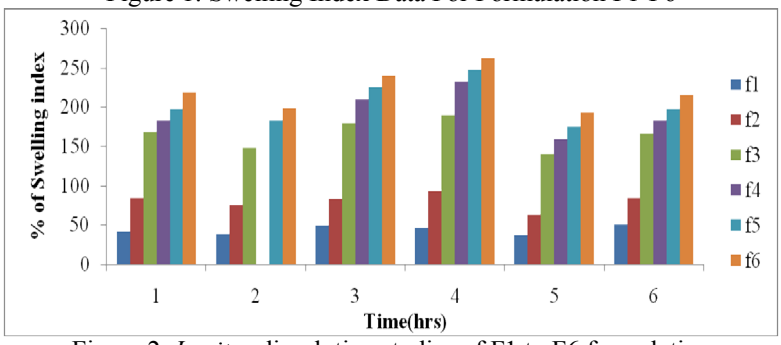

Figure 2: *In vitro* dissolution studies of F1 to F6 formulation

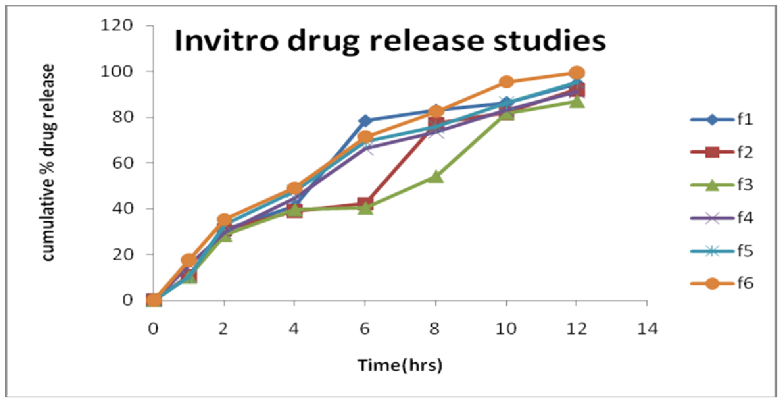

Table 5: Drug Content of the Formulations Developed Before and After Storage for 3 Months

Formulation Code	Percent Drug Content ($\overline{X}$ ± s.d)		Significance of Difference
	Before Storage	After 3 months	
F1	99.47 ± 0.07	98.23 ± 0.27	P > 0.05
F2	98.49 ± 0.06	97.08 ± 0.04	P > 0.05
F3	98.03 ± 0.11	97.90 ± 0.13	P > 0.05
F4	99.53± 0.37	98.03 ± 0.30	P > 0.05
F5	99.26 ± 0.86	98.02 ± 0.16	P > 0.05
F6	98.50 ± 0.81	97.90 ± 0.31	P > 0.05

Figure 3: Percent drug content of F6 formulation before and after storage

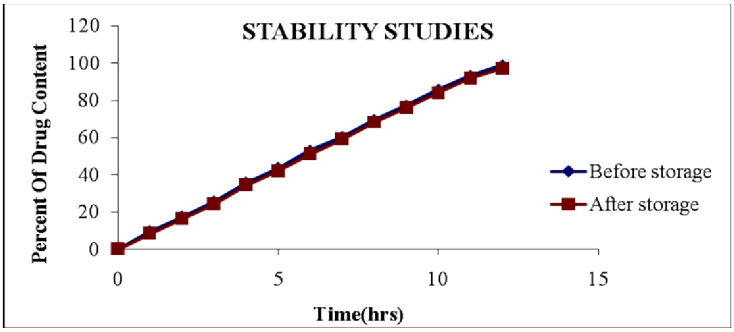

Table 6: *In vitro* buoyancy studies & drug polymer ratio

Formulation code	Floating lag time (min.)	Total floating time (Hrs.)	Drug polymer ratio
F1	02	>24	1:0.2
F2	03	>24	1:0.4
F3	04	>24	1:0.6
F4	03	>24	1:0.2
F5	04	>24	1:0.4
F6	02	>24	1:0.6

Fig 4: Floating of F6 formulation

REFERENCES:

1. Ballard, *B.E., "An* overview *of* prolonged action drug dosage forms. *In:* Robinson, J.R. *(*Ed*)*. Sustained *and* controlled release drug delivery systems"**,** Marcel Dekker, *Inc.* New York. *p: 501-528, 1978.*
2. DM Patel, Seed mucilage from ocimum americanum linn. As disintegrant in tablets: separation and evaluation. *Ind. J.Pharm.Sci*. vol69, issue 3, page no 431-435.
3. www.wikipedia.com.
4. Meghana S Kamble,. Evaluation of binding properties of ocimum tenuiflorum linn seed mucilage isolated by defatting method. *Journal of biomedical and pharmaceutical research,* 1(3); 22-27.
5. Kambe Meghana S. Mendake Satis. Studies on isolation and evaluation of ocimum tenuiflorum lin seed mucilage. *Journal of derug discovey and therapeutics*; 2(6), 25-28.
6. Prasad V.Kandam, Evaluation of acimum sactum and ocimum basilium mucilage as a pharmaceutical excipient, *Journal of chemical and pharmceuticl research*, 4(4):1950-1955.
7. T.Udaya Kumar, M.Vasudevan, Novel sustained release swellable bio adhesive floating gastro retentive drug delivery system of bilayer tablets containing rifampicin and isonoazid. *Int.J.Pharm.Sci*. 1;21-24
8. Lachman, L, Liberman, HA, and Kanig JL. The theory and practice of industrial pharmacy. 3rd Ed., Lea and Febiger, 1987, 297-300.
9. Hing mire L.P.(2008). Development and evaluation of sustained release matrix tablets using natural polymer as release modifier. *Research J. Pharm. Tech*., 1(3): 123.
10. Venkatesh D.N., Jawahar N.,Ganesh G.N.K., Kumar R.S., Senthil V., Samantha M.K., Sanker S. and Elango K. (2009). Development and in vitro evaluation of Sustained release matrix tablets of Theophylline using hydrophilic polymer as release rate retardant. *Int. J. Pharm. Sci.* Nano., 2(1): 34-38.
11. Mridanga R.R., Bose S.K. Sengupata K. (2008). Design, Development and in vitro evaluation of directly compressed sustained release matrix tablets of Famotidine. *Research J. Pharm . Tech.*, 1(3): 123.

How to cite this article:
S. Prasanthi , M.Vidyavathi*: Design and development of stomach specific drug delivery system of valsartan by using seed mucilage of ocimum bacilicum linn**:** 5(4): 2128-2133. (2014)