ISSN: 2230-7346

Yajaman Sudhakar et al. / JGTPS / 6(2)-(2015) 2589– 2595

(Research Article)

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

FORMULATION AND *IN VITRO* EVALUATION OF VALSARTAN SUSTAINED RELEASE TABLETS USING TAMARIND SEED POLYSACCHARIDE

Yajaman Sudhakar*[1], G. Satheesh[2], Jayaveera K.N[3]

[1]*Department of pharmacy, Govt. Polytechnic for Women, Kadapa, Andhra Pradesh, India.*

[2]*Department of Pharmaceutics, Sri Padmavathi School of Pharmacy, Tiruchanoor, Andhra Pradesh, India.*

[3]*Departmental of Pharmaceutical Chemistry, Oil and Technology Research Institute, Anantapur, Andhra Pradesh, India.*

ABSTRACT

The current learning was designed to develop sustained release antihypertensive tablets of Valsartan which acts as Angiotensin II receptor contender having a half life of 6 hrs with 25% bioavailability. The developed formulation provides the advantage of sustained release character thus maintaining therapeutic or tissue levels of drug for unmitigated period of time with fewer or no systemic unfavorable effects. Tamarind Seed Polysaccharide (TSP) was secluded from tamarind kernel powder and is a source obtained from Tamarindus indica. The obtained polysaccharide is used in preparation of tablets by wet granulation method and evaluated for its drug discharge characteristics. The optimized formulation is compared with that of additional naturally occurring polymers such as Guargum and Loctus bean gum. The formulated tablets were evaluated for its weight variation, thickness, hardness, friability, swelling index, and drug content. In vitro drug release studies indicate that among all the formulations VT3 significantly reduced the rate of drug release compared to other formulations. The results of dissolution studies shows that formulation VT3 show a maximum drug release of 61.33% by 12th hour and further extends its release rate. Mathematical handling of *invitro* drug release data suggest that, optimized formulation VT3 when built-in to zero order, first order, Higuchi, Korsmeyer-Peppas release kinetics gives an R^2 value of 0.995. Drug release from the formulation occurs by two mechanisms, swelling and erosion. Hence in assessment to Guar Gum and Loctus bean gum, Tamarind seed polysaccharide seem to be the finest sustained polymer to manage the discharge of Valsartan from its tablet formulation.

Key words: Valsartan, Tamarind Seed Polysaccharide, Guargum, Loctus bean gum, Sustained Release tablets.

INTRODUCTION:

Oral drug delivery has been acknowledged for decades as most extensively utilized path of administration among all other routes for systemic delivery of drugs which may be endorsed to its ease of administration. Sustained release of Valsartan tablets sustains the drug release and reduces the frequency of dosing and maintains plasma drug concentration in therapeutic window.

Address for correspondence

Dr. Yajaman Sudhakar
Senior Lecturer,
Department of pharmacy,
Govt. Polytechnic for Women, Kadapa – 516001, Andhra Pradesh, India
Email: yajamans@gmail.com

Valsartan is an angiotensin II receptor contender used in the treatment of hypertension, myocardial infarction and congestive heart failure. It acts by blocking the binding of angiotensin II and angiotensin I receptor in many tissues there by blocking the vasoconstrictor and aldosterone secretion outcome of angiotensin II selectively. The favored route of administering this drug is through oval cavity. The drug has a drawback of low solubility and low bioavailability (approximately 20-25%) with short half-life of (almost 6 hrs). As the drug has low solubility, low bioavailability and short half-life, the treatment for hypertension demands for longer duration by maintaining plasma concentration with constant drug release for longer duration, thus maintaining drug concentration in therapeutic window and increasing therapeutic efficacy of the drug.

The development of novel dosage form for drug delivery has resulted in the demand for novel

excipients to hold up the preferred properties, and polymers plays a crucial role in drug release. It's a monotonous process, highly expensive and time overwhelming in developing new excipients. There is always an increase in demand for plant based products as excipients due to its availability form natural source with low side effects, extensive availability, biocompatible, biodegradable and low cost with excellent substitute for man-made polymers. Majority of natural polymers has already gained their attention in various industries and are used in food industries, textile industries, tanneries, pharmaceutical industries as binders, gelling agents, disintegrants, film formers, suspending and emulsifying agents. There are various polysaccharides used in drug delivery system like cellulose esters[1] Loctus bean gum[2] Xanthan gum[3] Guargum [4] Pectin[5] Etc .in addition to these naturally occurring polymers Tamarind seed polysaccharide which is obtained from Tamarind seeds belonging to family Caesalpiniaceae find its existence in food, textile and paper industry possessing superior viscosity, non-carcinogenicity, mucoadhesive nature, extensive pH acceptance, biocompatible and biodegradable.[6] It consists of about 65% of seed components, and branched polysaccharide with main chain length consisting of β-d-(1,4)-linked glucopyranosyl units, with side chain of single d-xylopyranosyl unit attached to second, third and fourth d-glucopyranosyl unit through an □-d-(1,6) linkage. One d-galactopyranosyl unit is attached to one of xylopyranosyl units through β-d-(1,2)-linkage.[7] Tamarind seed polysaccharide has notable characters like lofty puffiness property, glueyness, high viscosity etc.[8-11]. Hence the aim of this proposed work is to formulate, characterize and assess sustained release tablets of Valsartan to obtain desired drug release, better patient compliance, reduce dosing frequency, and cost efficiency dosage form and to evaluate the practicability of using tamarind seed polysaccharide as a polymer for sustained release drug delivery system.

MATERIALS AND METHODS:

Valsartan was obtained as a gift sample from Zydus Cadilla; Tamarind Seed (TSP) procured from local market, Guar gum was purchased from S. Kanth. Health care ltd. Vapi. Gujarath. Loctus bean gum was obtained as gift sample from Sooraj Chemicals, Gujarath, and Microcrystalline cellulose pH 101 was purchased from S.D.Fine chemicals and all other reagents were of analytical grade.

Separation of TSP from Tamarind seeds

The procured seeds of Tamarindus indica are washed with water to remove any adhered material. The washed seeds were heated on a hot pan at a temperature of 70°C for 45 min and the seeds were made free from testa and are crushed. The crushed seeds were boiled in water for 2-3 hrs and kept aside overnight to release the mucilaginous content into water which is collected after filtration. To the filtrate equal quantity of ethanol is added to split mucilage as precipitate. The precipitated material is dried in hot air oven at a temperature of 50°C for 3 hours. The dried product is pulverized into powder and stored in airtight container till further use.[12]

Construction of Standard Graph of Valsartan

Accurately weighed amount of 100 mg valsartan was transferred into a 100ml volumetric flask, dissolved in pH 6.8 phosphate buffer and the volume was made up to 100 mL with the same phosphate buffer. The resulted solution had the concentration of 1mg/ml which was labeled as 'stock'. From this stock solution 10ml was taken and diluted to 100 mL with phosphate buffer which has given the solution having the concentration of 100 mcg/ml. Necessary dilutions were made by using this second solution to give the different concentrations of valsartan (5to 35 mcg/mL) solutions **Table: 2**. The absorbances of above solutions were recorded at 249 nm of the drug using double beam UV-Visible spectrophotometer. Standard graph was plotted between the concentration on X-axis and absorbance on Y-axis **Fig: 1**.

FORMULATION OF VALSARTAN TABLETS:

The tablets were prepared by wet granulation method using water as granulation solution. All the required ingredients were weighed accurately and passed through sieve # 85. To the weighed content required amount of granulating solution (water) is added and mixed well. The wet mass is passed through sieve # 12 to obtain uniform granules which are then dried at 50°C for 3 hours. Magnesium stearate is added as lubricant to the final dried granules and blended for few minutes which are then compressed into tablets of 200 mg average weight using rotary tablet press. The composition for the tablet preparation is listed in **Table: 1**.

EVALUATION PARAMETERS:

Weight Variation Test:

To study weight variation, individual weights (W_I) of 20 randomly selected tablets from each formulation were weighed using electronic balance and their average weight (W_A) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated.

$$\% \text{ weight variation} = \frac{WA - WI}{WA} \times 100$$

Thickness:

Ten tablets from the respective sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper. Average thickness and standard deviation values were calculated.

Hardness test:

Tablet hardness was measured by using Pfizer hardness tester. From each batch six tablets were measured for the hardness and average of six values was noted along with standard deviations.

Friability Test:

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, dedusted and reweighed. The friability was calculated as the percentage weight loss as follows.

$$\% \text{ Friability} = \frac{W_1 - W_2}{W_1} \text{ X } 100$$

Where W_1 = Initial weight of the 10 tablets.

W_2 = Final weight of the10 tablets after study.

Friability values below 1.0% are generally acceptable as per pharmacopoeial standards.

Measurement of swelling index:

Swelling index (S.I.) is the phenomenon of ability of polymer to hydrate and estimate the degree of solvent diffusion into the tablet which is resolute by equilibrium weight gain method. The tablets were accurately weighed and placed in petri dish containing of pH 6.8 phosphate buffer (dissolution medium). At regular time intervals the tablets were removed from petri dish and the tablets were blotted using tissue paper to remove excess free liquid and are reweighed. The SI of each tablet was calculated as follows.

$$\text{S.I.} = \frac{W_t - W_0}{W_0} \text{ X } 100$$

Where W_0 = Initial weight of tablet

W_t = Final weight of tablet.

***In -Vitro* Drug Release Characteristics**

Drug release was assessed by dissolution test under the following conditions: n = 3, eight station dissolution rate test apparatus (Electrolab) USP type II dissolution apparatus (paddle method) at 50 rpm in 900 ml of the pH 6.8 phosphate buffer till 12 hours, maintained at 37°C ± 0.5°C. An aliquot (5ml) was withdrawn at pre determined time intervals, were filtered through Whattsmann filter paper 0.45µ and assayed for Valsartan UV-Spectrophotometrically at 249 nm. The samples of dissolution fluid withdrawn at each time interval were replaced with the same volume of pre warmed (37°C ± 0.5°C) fresh drug free dissolution medium and a suitable correction was made for the amount of drug present in the samples withdrawn.

RESULTS AND DISCUSSION:

Standard Graph of Valsartan:

The standard graph of valsartan prepared showed good linearity with R^2 values 0.998 in pH 6.8 phosphate buffer, which suggests that it obeys the "Beer-Lambert's law".

Characterization of Tablets

Evaluation of the Prepared Tablets for Physical Parameters

Sustained release matrix tablets of valsartan containing different compositions were prepared by wet granulation method and tested for physicochemical parameters like uniformity of weight, hardness, thickness, friability and content uniformity. The results of the tests are shown in **Table: 3.** all the tablets of different batches complied with the official requirements of uniformity of weight as their weights varied between 198.41 and 201.54 mg. The Thickness of the tablets ranged from 4.19 to 4.38mm. The hardness of the tablets ranged from 5.19 to 5.80 kg/cm^2 and the Friability values were less than 1.0% indicating that the tablets were compact and hard. Swelling index for the tablets ranges from 0.026 to 2.98. All the formulations satisfied the content of the drug as they contained 96 to 101% of Valsartan. Thus all the physical attributes of the prepared tablets were found to be practically within standards.

***In-Vitro* Drug Release Studies:**

Sustained release tablets of valsartan containing TSP, Guar gum and Loctus bean gum were subjected to *invitro* drug release studies. Dissolution rate of Valsartan tablets prepared was studied in pH 6.8 Phosphate buffer (900 ml) employing using paddle stirrer at 50 rpm and at a temperature of 37°C ± 0.5°C. The experiment was run in triplicate (n=3). The cumulative percent of drug released at different time intervals are given in **Table: 4.** A graph was plotted between Average % Drug Release Vs Time **Fig: 2**. All the formulations showed the burst release of valsartan within 10 - 15 minutes interval.

Formulations of Valsartan containing TSP retarded the drug release as a function of polymer concentration VT1, VT2 and VT3 showed the cumulative % drug release of 74.87, 68.12 and 61.33 for 12 hrs in a controlled manner without changing their physical integrity in dissolution medium. Formulations VG and VL showed the cumulative % drug release of 76.93 and 70.17 within 12 hrs. TSP, Guar gum and Loctus bean gum being hydrophilic polymer upon contact with aqueous fluid form viscous gel, and hence retard the drug release. Correlation Coefficient (r) values in the analysis of the release data as per Zero, First Order, Higuchi and Peppas equation model are presented in Table: 5.

Fourier transforms infrared spectroscopy (FTIR)

FTIR spectra of Valsartan pure drug, formulations containing valsartan polymers are shown in figures 3-7**.** The characteristic peaks of the formulations followed the same path as that of the drug alone. Hence the FTIR studies clearly indicated that there is no drug polymer interaction.

Table: 1 Formulation of Valsartan Sustained Release Tablets.

CODE	Drug (mg)	TSP (mg)	Guar Gum (mg)	Loctus bean gum (mg)	MCC (mg)	Mg. Stearate (mg)	Total Weight (mg)
V	80	-	-		119.9	0.1	200
VT1	80	20	-		99.9	0.1	200
VT2	80	40	-		79.9	0.1	200
VT3	80	80	-		39.9	0.1	200
VG	80	-	80		39.9	0.1	200
VL	80	-	-	80	39.9	0.1	200

V- Valsartan, VT – Valsartan with TSP, VG – Valsartan with Guar gum, VL – Valsartan with Loctus bean gum

Table: 2 Standard Graph of Valsartan

Concentration (mcg/ml)	Absorbance
	pH 6.8 Phosphate Buffer
5	0.190
10	0.342
15	0.483
20	0.632
25	0.785
30	0.964
35	1.14
R^2	**0.998**

Table: 3 Physico chemical Evaluation of Sustained Release Matrix tablets of Valsartan

F. Code	Weight variation ± S.D	Thickness (mm) ± S.D	Hardness (kg/cm^2) ± S.D	Friability (%) ± S.D	Swelling Index	Drug content ± S.D
V	201±0.54	4.26±0.17	5.80±0.44	0.34±0.02	0.026	99.15±1.22
VT1	198±1.48	4.19±0.25	5.45±0.34	0.37±0.15	1.14	96.26±0.83
VT2	198±0.41	4.37±0.82	5.25±0.48	0.49±0.02	2.26	98.92±2.19
VT3	198.8±1.64	4.27±0.22	5.53±0.35	0.25±0.48	2.98	101.26±0.86
VG	200.6±1.14	4.19±0.36	5.49±0.59	0.59±0.14	0.96	100.34±1.17
VL	199.2±0.83	4.38±0.22	5.19±0.38	0.63±0.09	0.83	98.55±1.93

Table: 4 Average % Drug Release of Valsartan tablets

Time (hrs)	V	VT1	VT2	VT3	VG	VL
0	0	0	0	0	0	0
0.25	10.12	9.46	8.24	3.54	13.88	11.78
0.5	18.67	11.92	10.55	4.62	15.45	13.16
1	34.63	16.45	12.67	6.74	20.22	14.88
1.5	41.32	19.77	14.42	10.93	26.89	17.81
2	50.88	24.33	19.63	12.89	29.88	24.92
4	57.84	32.27	21.79	22.18	36.71	35.22
6	68.93	38.76	49.01	28.72	44.16	42.67
8	76.79	56.77	52.15	41.65	68.74	66.73
12	92.73	74.87	68.12	61.33	94.93	98.17

Table: 5 Correlation Coefficient (r) values

Formulation	Zero Order		First Order			Higuchi	Korsmeyer-Peppas
	R^2	K_0	R^2	K_1	$t_{1/2}$	R^2	N
V	0.841	6.903	0.968	-0.19	3.58	0.972	0.532
VT3	0.995	4.908	0.976	-0.07	9.71	0.931	0.752
VG	0.963	6.947	0.857	-0.20	3.38	0.935	0.483
VL	0.98	7.417	0.789	-0.27	2.59	0.914	0.55

Fig. 1 Standard graph of valsartan in 6.8 pH Buffer

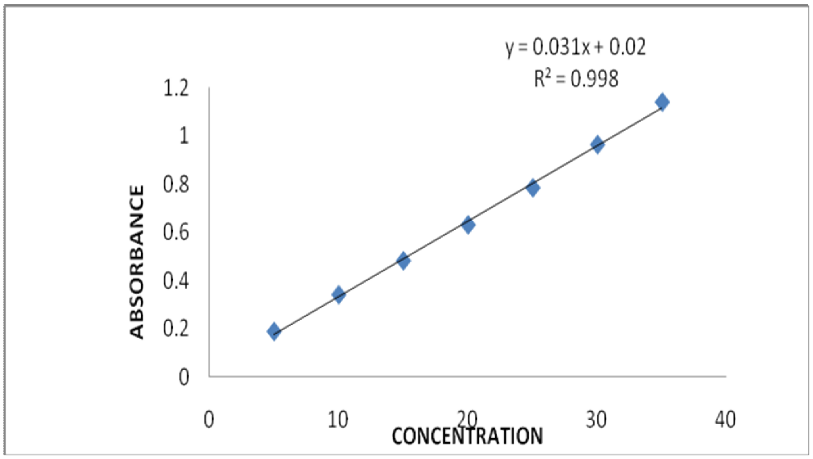


Fig: 2 Average % Drug Release Vs Time

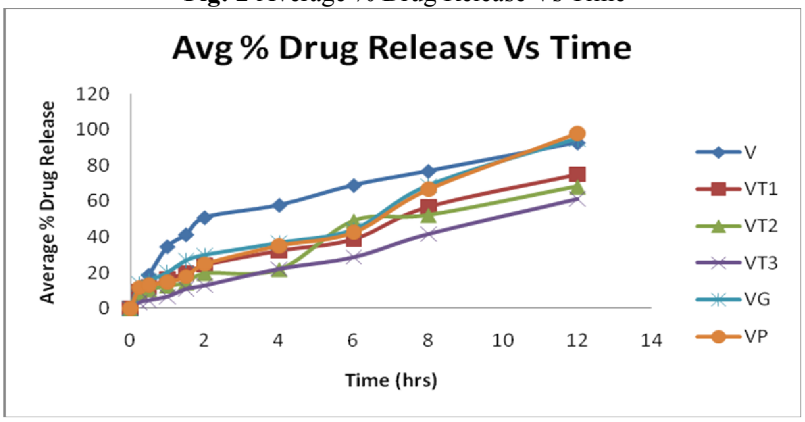


Fig: 3 FTIR Spectra of Valsartan

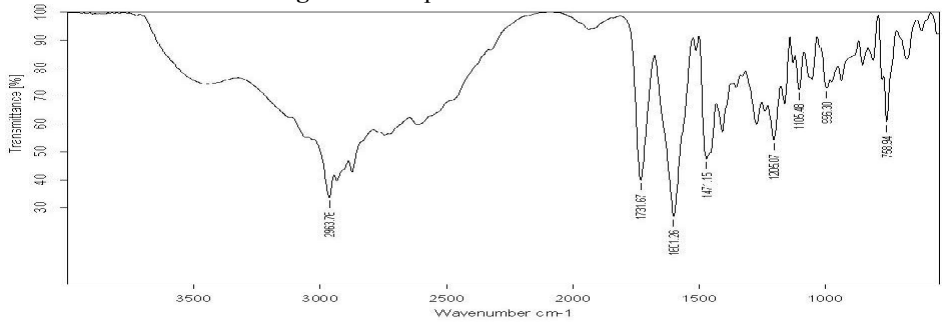


Fig: 4 FTIR Spectra of TSP

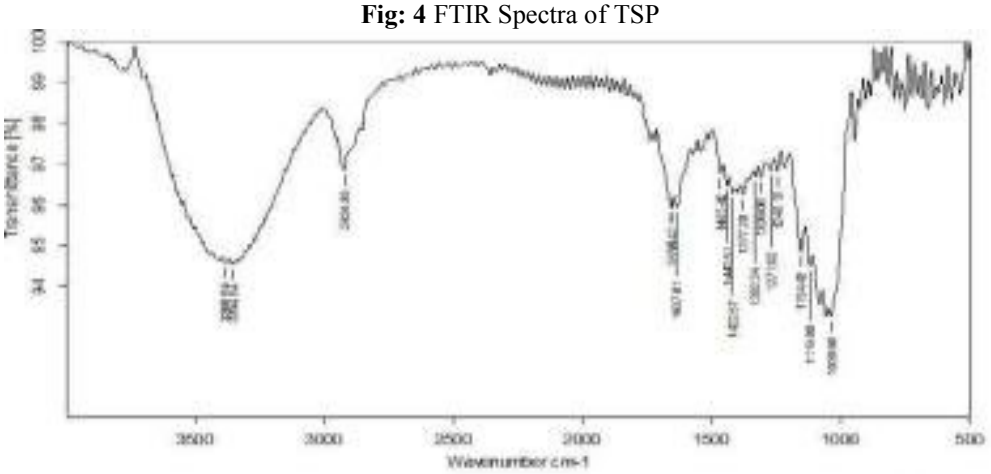


Fig: 5 FTIR Spectra of Formulation VT3

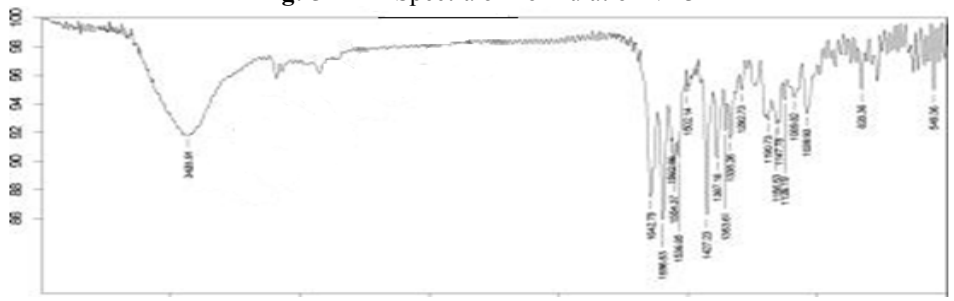


Fig: 6 FTIR Spectra of Formulation VG

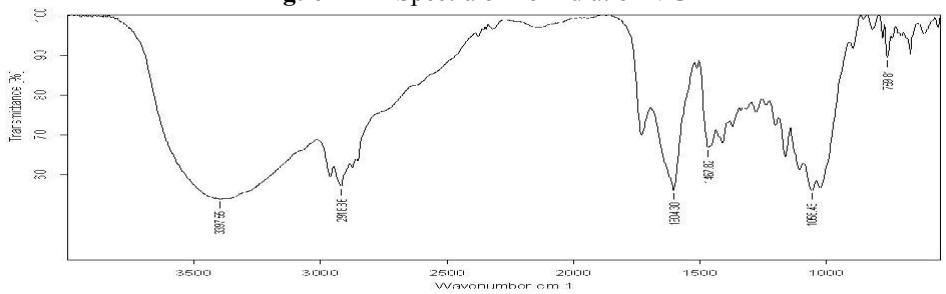
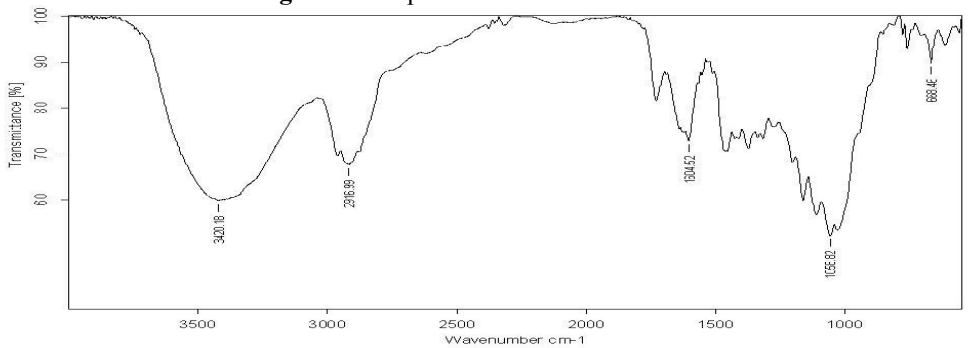


Fig: 7 FTIR Spectra of Formulation VL



REFERENCES:

1. Ford JL and Edgar PJ., Importance of drug type, tablet shape and added diluents on drug release kinetics form hydroxypropyl methylcellulose matrix tablets, Int.J.Pharm, 1987, 40, 223.
2. Sujja-areevath J, Munday DL, Cox PJ, Khan KA., Release characteristics of Diclofenac sodium from encapsulated natural gum mini-matrix formulations, Int.J.Pharm, 1996, 139, 53.
3. Talukdar MM., Evaluation of Xanthan gum as a hydrophilic matrix for controlled release dosage form preparations, Drug Dev. Ind.Pharm., 1993, 19, 1043.
4. Sano M, Miyata E, Tamano S, Hagiwara A, Ito N, Shirai T., Lack of carcinogenicity of tamarind seed polysaccharide in B6C3F mice, Food Chem. Toxicol.,1996, 34, 463-67.
5. Vyas SP and Khar RK. Controlled Drug Delivery and Advances. 1st edition. Delhi, Vallabh Prakashan 2005; 155-195.
6. Rao PS and Srivastava HC., Tamarind in industrial gums. In: Whistler RL. 2 nd ed., Academic Press, New York, 1973, 369-411.
7. Gidley MJ, Lillford PJ, Rowlands DW. Structural and solution properties of tamarind- seed polysaccharide, Carbohydrate Res., 1991, 214, 299-314.
8. Kulkarni D, Dwivedi AK, Sarin JPS and Singh S. Tamarind seed polyose: A potential polysaccharide for sustained release of verapamil hydrochloride as a model drug. Indian J Pharm Sci. 1995; 59(1):1-7..
9. Kulkarni D, Dwivedi A. and Singh S. Performance evaluation of tamarind seed polyose as a binder and in sustained release formulations of low drug loading, Indian J Pharm Sci. 1998; 1:50-3.
10. Bhavin P, Piyush P, Ashok B, Shrawaree H and Swati M. Evaluation of tamarind seed polysaccharide as a mucoadhesive and sustained release component of Nifedipine buccoadhesive tablet & comparison with HPMC and Na CMC. Int Journal of Pharm Tech Res. 2009; 1(3):404-9.
11. Sumathi S and Alok RR. Release behavior of drugs from tamarind seed polysaccharide tablets. J Pharm Pharmaceut Sci. 2002; 5(1):12 -8.
12. Rao PS, Ghosh TP, Krishna S., Extraction and purification of tamarind seed polysaccharide, J. Sci Ind Res., 1946, 4, 705.

How to cite this article:

Yajaman Sudhakar *, G. Satheesh, Jayaveera K.N, Formulation and in *Vitro* evaluation of valsartan sustained release tablets using tamarind seed polysaccharide, 6 (2): 2589 – 2595 (2015)