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Formulation and Evaluation of Gastroretentive Bosentan Monohydrate Tablets Using Raft Technology

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ABSTRACT

The objective of the present study is to develop Bosentan monohydrate gastric tablets using raft technology with the aim to achieve controlled drug release for the treatment of Pulmonary Arterial Hypertension (PAH). Floating tablets were prepared by direct compression method using different concentrations of xanthum gum, chitosan, Carbopol 934 and methocel E15. Pectin is used as raft forming agent. Drug, polymer and pectin were taken in different ratios like (2:1:1); (1:1:1); (2:2:1). Drug-excipient compatibility study showed no interaction between drug and excipients. Stability study of the optimized formulation showed that the tablets were stable at accelerated environmental conditions for 2 months.The prepared formulations were subjected to pre-compression parameters like angle of repose, bulk density, tapped density, Hausner's ratio, Carr's index and post-compression parameters like hardness, floating lag time, floating time and disintegration. All the formulations resulted in acceptable Pharmacopoeia limits. Tablets were subjected to *In-vitro* drug release in 0.1 N HCl (pH 1.2) for 12 hours. Among the different combinations of polymers in different ratios studied, F11 was found to be the best formulation showing 99.9% *in-vitro* drug release which includes drug, polymer, and pectin in the ratio of 2:1:1 respectively. Hence from this study, it can be concluded that pectin can be used as raft forming agent for controlling the drug release.

INTRODUCTION

Bosentan is an endothelin receptor antagonist (ERA), prescribed for pulmonary arterial hypertension. Pulmonary arterial hypertension (PAH) is a progressive disease caused by narrowing or tightening (constriction) of the pulmonary arteries, which connects the right side of the heart to the lungs. The medication blocks the effects of endothelin-1 (ET-1), thereby decreases blood pressure in lungs. The medication also inhibits the blood vessel thickness. Endothelin-1 is a neurohormone, the effects of which are mediated by binding to ETA (Endothelin receptor type A) and ETB (Endothelin receptor type B) receptors in the endothelium and vascular smooth muscle. ET-1 concentrations are elevated in plasma and lung tissues of patients with pulmonary arterial hypertension, suggesting a pathogenic role for ET-1 in this disease. Bosentan is a specific and competitive antagonist at endothelin receptor types ETA and ETB. Bosentan has a slightly higher affinity for ETA receptors than for ETB. It is better than other endothelin receptor antagonists. After oral administration, the drug is rapidly and extensively absorbed. It is rapidly distributed, extensively bound to albumin and eliminated with a terminal half-life of about 5 hrs. Excretion of unchanged drug in urine and feces is negligible. These characteristics makeBosentan a candidate for incorporation in a controlled-release dosage form.

Raft-forming systems

A simple meaning of Raft is a flat structure, typically made of planks, logs, or barrels, that floats on water and is used for transport or as platform for swimmers. Here also we are considering something that floats on the gastric content of stomach. The mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. This raft floats on gastric fluids because of low bulk density created by the formation of CO_2.Usually, the system contains a gel-forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO_2 to make the system less dense and float on the gastric fluids. The system contains a gel-forming agent (e.g. alginic acid), sodium bicarbonate and acid neutralizer, which forms a foaming sodium alginate gel(raft) when in contact with gastric fluids. The raft thus formed floats on the gastric fluids and prevents the reflux of the gastric contents (i.e. gastric acid) into the esophagus by acting as a barrier between the stomach and esophagus.

MATERIALS AND METHODS:

MATERIALS: Bosentan monohydrate was obtained from Natco Research Centre, Hyderabad as a gift sample. Carbopol 934, Xanthan gum, Chitosan, Methocel E15, and pectin were used in the preparation of raft-forming tablets. All other excipients used were of a standard pharmaceutical grade.

METHODS:

Preparation of stock solution

100mg of Bosentan monohydrate was accurately weighed using contech digital balance and then transferred to 100ml of volumetric flask. To this little amount of 0.1N HCl was added and mixed properly to dissolve the drug and made up to the mark by using 0.1N HCl to give 1000µg/ml (stock solution).

Standard calibration of Bosentan in 0.1N HCl

From the stock solution 10ml was taken and transferred to 100ml volumetric flask and made up to the mark with 0.1N HCl to prepare 100µg/ml which is called as working standard I. From the working standard I, 10 ml was pipetted out into 100ml volumetric flask and made up to the mark with 0.1N HCl to prepare 10µg/ml which is called as working standard II. From the working standard II dilutions were made using 2,4,6,8 and 10 ml of the solution to give 2,4,6,8 and 10µg/ml respectively. The absorbance of these solutions was measured against the blank at λ_{max} 242nm using double beam UV spectrophotometer.The method was validated for linearity, accuracy, precision. From the obtained absorbance, the calibration curve was plotted by taking concentration on X-axis and absorbance on Y-axis.

DRUG-EXCIPIENT COMPATIBILITY BY FTIR STUDIES

In the preparation of controlled release tablet, drug and polymer may interact as they are in close contact with each other, which could lead to instability of drug.Preformulation studies regarding drug-polymer interactions are therefore very critical in selecting appropriate polymers. FT-IR spectroscopy was employed to ascertain the compatibility between bosentan and selected polymers. The individual drug and drug with excipients were scanned separately.

Procedure

Completely dried potassium was transferred into a mortar. About 2% of pure drug or with excipients was weighed in a digital balance, mixed and ground to a fine powder. Two stainless steel discs were taken out of the desiccator. A piece of the pre-cut cardboard on top of one disc was placed and cut out hole was filled with the finely ground mixture. The second stainless steel disc was kept on top and transfers the sandwich onto the pistil in the hydraulic press. With a pumping movement, hydraulic pump handle moved downward. The pistil will start to move upward until it reaches the top of the pump chamber. Then, the pump handle moved upwards and continued pumping until the pressure reaches 20,000 prf. Rest for a few seconds and with the small lever on the left side, the pressure was released. Removing of the discs and pulling apart. The obtained film was homogenous and transparent in appearance. Then inserted into the IR sample holder and attach with scotch tape and run the spectrum.

EVALUATION OF PRE-COMPRESSION PARAMETERS

Angle of repose

The angle of repose of blends was determined by the funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the blend. The blend was allowed to flow from the funnel on the surface. The diameter and height of the heap formed from the blend were measured. The angle of repose was calculated using following formula.

$\text{Tan}\theta = h/r$

Where "h" is a height of the heap and "r" is the radius of the heap of blends.

Bulk Density (BD)

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The volume occupied by the powder was measured which gave bulk volume.

Tapped bulk density (TBD)

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The measuring

cylinder was tapped until no further change in volume was noted which gave the tapped volume.

Carr's compressibility index

The Carr's compressibility Index was calculated from Bulk density and tapped density of the blend. A quantity of 2g of a blend from each formulation was filled into a 10mL of measuring cylinder. Initial bulk volume was measured and the cylinder was allowed to tap from the height of 2.5cm. The tapped frequency was 25±2 per min to measure the tapped volume of the blend. The bulk density and tapped density were calculated by using the bulk volume and tapped volume.Compressibility index was calculated using the following formula:

$$\% \text{ Compressibility index (I)} = \frac{\text{Tapped density } (D_t) - \text{Bulk density } (D_b)}{\text{Tapped density } (D_t)} \times 100$$

PREPARATION OF RAFT FORMING TABLETS BY DIRECT COMPRESSION METHOD

Drug, polymer and other ingredients were weighed accurately. All ingredients were passed through 80 mesh. The passed ingredients were mixed thoroughly except the binder and lubricant. Binder and lubricant were added before the compression. The powder was poured into the die and compressed into the tablet.

Table 1: Different formulations for optimization of polymer and pectin

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Bosentan monohydrate	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
Sodium bicarbonate	45	45	45	45	45	45	45	45	45	45	45	45
Starch	30	30	30	30	30	30	30	30	30	30	30	30
Pectin	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	31.25	31.25	31.25	31.25
Chitosan	-	62.5	-	-	-	31.25	-	-	-	31.25	-	-
Xanthan gum	62.5	-	-	-	31.25	-	-	-	31.25	-	-	-
Methocel E15	-	-	-	62.5	-	-	-	31.25	-	-	-	31.25
Carbopol	-	-	62.5	-	-	-	31.25	-	-	-	31.25	-
Lactose monohydrate	20	20	20	20	20	20	20	20	30	30	30	30
Magnesium stearate	5	5	5	5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Microcrystalline cellulose	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Talc	5	5	5	5	5	5	5	5	6	6	6	6
Total(mg)	300	300	300	300	270	270	270	270	250	250	250	250

EVALUATION OF TABLETS

Hardness test

Hardness indicates the ability of a tablet to withstand mechanical strength while handling. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm2.Three tablets were randomly picked from each formulation and the mean and standard Deviation values were calculated.

Friability test

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (Wt.initial) and transferred into friabilator. The friabilator was operated at 25 rpm for4 minutes or run up to 100 revolutions. The tablets were weighed again (Wt.final).

Weight variation test

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. To study weight variation, 20tablets of each formulation were weighed using an electronic balance and the test was performed according to the official method.

Floating lag time

The buoyancy lag time was determined in the U.S.P. dissolution test apparatus II in the acid environment. The time interval between the introduction of the tablet into the dissolution medium and its buoyancy to the top of the dissolution medium is buoyancy lag time or floating lag time.

Raft strength measurement by in-house method

A tablet powder equivalent to unit dose was transferred to150 mL of 0.1 N HCl maintained at 37°Cin a 250 mL glass beaker. Each raft was allowed to form around an L-shaped wire probe (diameter: 1.2 mm) held upright in the beaker throughout the whole period (30 min) of raft development. Raft strength was estimated using the modified balance method. Water was added dropwise to the pan and the weight of water required to break the raft was recorded. A double pan dispensing balance was modified for raft strength measurement. One pan of the dispensing balance was replaced with an L-shaped wire probe as shown in Figure 1.

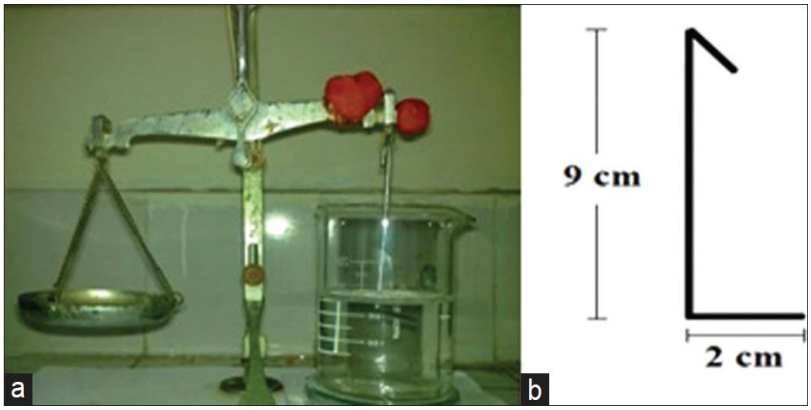


Fig. 1: (a) Modified balance method (b) Wire probe for raft strength measurement

***In-vitro* drug release studies**

Drug release from the prepared tablets was determined up to 12hrs using USP type II (paddle type) dissolution test apparatus. 0.1 N HCl (900 ml) was used as dissolution medium.The paddle was adjusted at 50 rpm and the temperature of 37±0.5°C was maintained throughout the experiment.Samples were withdrawn at known time intervals and were replaced with the same volume of fresh dissolution media after each withdrawal. The samples were analyzed for drug contents by measuring absorbance by using UV spectrophotometer.

Dependent-model method (Data analysis)

In order to describe the Bosentan release kinetics from individual tablet formulations, the corresponding dissolution data were fitted in various kinetic dissolution models: zero order, first order, Higuchi, Korsmeyer-Peppas. When these models are used and analyzed in the preparation, the rate constant obtained from these models is an apparent rate constant. The release of drugs from the matrix tablets can be analyzed by release kinetic theories. To study the kinetics of drug release from matrix system, the release data were fitted into Zero order as the cumulative percentage of drug release vs. time (Eqn.1), first order as log cumulative percentage of drug remaining vs. time (Eqn.2), Higuchi model as cumulative percent drug release vs. square root of time (Eqn.3). To describe the release behavior of the polymeric systems, data were fitted according to well known exponential Korsmeyer – Peppas equation as log cumulative percent drug release vs log of time equation (Eqn.4).

(i) Zero-order kinetics

$Qt=K_0t$……(1)

Where,

Q= Amount of drug release in time t

K_0 = Zero order rate constant expressed in unit of concentration /time

t = Release time

(ii) First order kinetics

Log $Q=\text{Log } Q_0-kt/2.303$.....(2)

Where,

Q_0= is the initial concentration of drug

k= is the first order rate constant

t =release time

(iii) Higuchi kinetics

$Q=kt_{1/2}$.....(3)

Where,

k= Release rate constant

t=release time,

Hence the release rate is proportional to the reciprocal of the square root of time.

(iv) Korsmeyer-Peppas

First, 60% *in-vitro* release data were fitted in an equation of Korsmeyer-peppas to determine the release behavior from controlled release polymer matrix system. The equation is also called a power law,

$M_t / M_\infty = Kt\ n$.....(4)

Where,

M_t = amount of drug released at time t

M_∞ = amount of drug released after infinite time

M_t / M_∞ = fraction solute release

t = release time

K = kinetic constant incorporating structural and geometric characteristics of the polymer system

n = diffusional exponent that characterizes the mechanism of the release of traces.

The magnitude of the release exponent "n" indicates the release mechanism (i. e. Fickian diffusion, Non-Fickian, super case II release).For floating tablets, values of n near 0.5 indicates Fickian diffusion controlled drug release and n value near 1.0 indicates erosion or relaxational control (case II relaxational release transport, non-Fickian, zero order release). Values of n between 0.5 and 1 regarded as an indicator of both diffusion and erosion as overall release mechanism commonly called as the anomalous release mechanism.

STABILITY STUDIES:

Stability studies were conducted according to ICH guidelines. Optimized tablets (formulation F11) were stored under 40±2°C/75%RH in the humidity chamber for a period of 3 months. After 3 months, the tablets were tested for *in vitro* drug release studies, weight variation, friability, hardness and floating time.

RESULTS AND DISCUSSION:

Analytical Method for Construction of calibration curve

In order to conduct the *in vitro* drug dissolution studies, the calibration curve was plotted to determine R^2 and the equation of a straight line is used to calculate drug release. Calibration curve ofBosentan monohydrate in 0.1 N HCl (pH 1.2) was constructed against the respective buffer as blank at λ_{max} of 242 nm and are represented in "Fig.2".

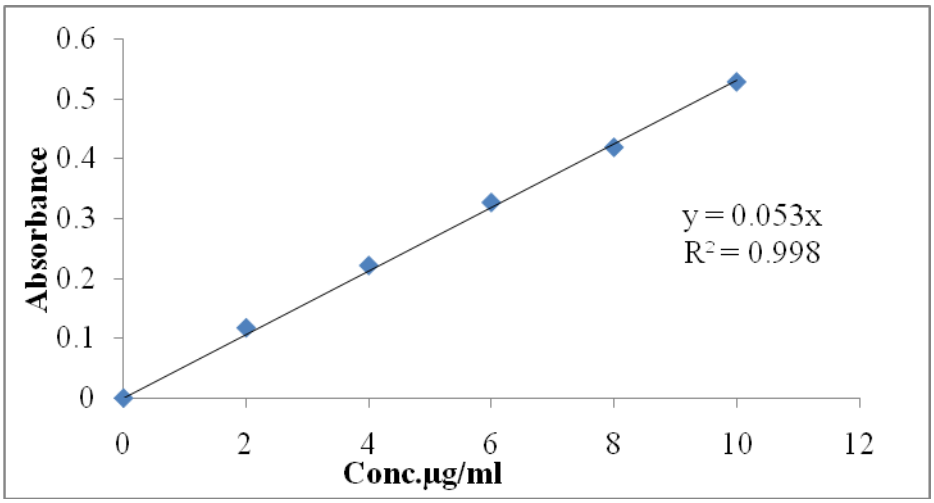


Fig 2. Standard curve of Bosentan monohydrate in 0.1N HCL

Preformulation study

The angle of repose for a pure drug was very high and hence the poor flow of drug was exhibited whereas the angle of repose of formulations was very less showing good flow. The Carr's index of the pure drug was found to be high confirming that the drug has poor flow property and compressibility.

Table 2: Pre-formulation studies of all the formulations

Parameters	Angle of repose (°)	Bulk density(g/cc)	Tapped density(g/cc)	Hausner's ratio	Carr's compressibility index
F1	28.2±0.15	0.74±0.25	0.87±0.12	1.09±1.23	9.05±0.15
F2	31.5±1.25	0.49±0.15	0.56±0.12	1.12±1.57	11.1±0.125
F3	30.2±0.55	0.47±0.82	0.58±1.25	1.11±1.38	10.5±0.42
F4	29.0±1.27	0.56±0.87	0.64±1.55	1.14±1.22	12.5±0.14
F5	29.1±1.65	0.59±0.54	0.62±1.69	1.03±0.54	14.95±1.02
F6	24.1±1.58	0.45±0.98	0.64±2.36	1.54±1.25	11.6±1.25
F7	24.6±1.56	0.45±0.65	0.64±2.48	1.62±2.36	26.6±2.03
F8	26.5±1.84	0.54±1.58	0.56±2.65	1.08±2.35	5.55±1.54
F9	25.5±2.23	0.54±1.98	0.76±2.88	1.45±1.32	29.19±2.04
F10	27.1±1.26	0.59±1.66	0.59±1.25	1.62±1.25	11.69±1.02
F11	25.13±1.65	0.528±1.25	0.599±1.08	1.13±1.02	11.52±1.02
F12	28.2±2.35	0.58±0.64	0.68±1.86	1.98±0.24	19.65±1.02

All the values are expressed as mean ± S.D. n=3

Post-compression parameters

The hardness of the tablets was found to be between 3-4 kg/cm^2 and % friability of tablets ranged between 0.01 and 0.08%. The tablets have enough hardness to withstand stress during the transport and handling.

Table 3: Table showing post-compression parameters' values

Formulations	Disintegration time(sec)	Hardness (kg/cm²)	Floating lag time(sec)	Floating time(hrs)	Raft strength(gms)
F1	48.33±2.94	3.33±1.25	24±1.27	12.3±0.47	4.2±0.12
F2	40±1.08	3.5±0.74	11.33±1.25	12.3±1.25	2.6±0.15
F3	391.3±2.3	3.79±0.85	7.67±1.25	13.67±1.25	2.5±0.11
F4	320.67±2.5	3.243±0.77	19.67±2.05	14±1.63	4.9±0.02
F5	40.67±0.9	3.273±0.43	23.33±2.68	14±0.82	4.6±0.65
F6	50.67±1.25	2.97±0.62	17±2.16	14.3±1.7	4.8±0.12
F7	383.67±2.7	3.63±0.48	13±2.94	15.3±0.47	3.5±1.65
F8	334.67±1.18	3.863±0.3	22.67±2.05	14.3±0.47	4.1±1.24
F9	38±1.35	3.5±0.52	14.67±2.05	14.67±0.47	5.2±1.25
F10	45±2.74	3.813±0.69	14±0.82	13±0.82	4.9±0.36
F11	394.67±1.5	4.573±0.74	16±0.82	15±0.82	5.6±1.45
F12	337.67±1.4	4.48±0.55	21±1.63	13.3±1.25	4.8±1.32

All the values are expressed as mean ± S.D. n=3

***In vitro* drug release profile of Bosentan monohydrate tablets**

According to the formulations mentioned in table 1, Bosentan monohydrate tablets were prepared and subjected to dissolution studies. 12 formulations were developed by using different ratios of excipients and polymers. According to all the formulations, F11 has shown ideal drug release. In this particular formulation, carbopol is used as polymer and other excipients are used in the same ratio when compared to other formulations. Sodium bicarbonate is used as effervescent which helps to float the tablet immediately. As a result, it leads to the evolution of CO_2 gas resulting in low density. Thus, the tablet will float.

Table 4: Drug release profile of Bosentan monohydrate

Time (hrs)	F1	F2	F3	F4	F5	F6
0.5	7.58±0.8	8.1±0.7	5.76±0.5	7.29±1.2	14.7±0.9	15.7±0.64
1	13.1±1.2	17.4±0.8	16.14±1.8	12.6±0.8	25±1.6	27.58±0.6
2	24.4±0.6	22.7±1.0	25.7±1.2	16.1±1.2	33.3±1.4	33.38±0.53
3	34.3±1.1	26.6±0.8	28.4±0.7	24.3±0.9	38.5±08	39.38±1.96
4	35.4±1.3	32.6±0.9	32±0.4	29.2±1.3	46.2±08	44.18±3.3
5	36±0.95	34.9±0.5	33.2±0.4	31.2±0.8	49.2±0.8	49.25±1.0
6	37.3±0.4	37.8±1.5	35.5±0.8	33±0.5	55.1±1.1	54.34±2.0
7	38.5±0.8	41.5±1.0	38.6±0.9	35.2±2	56.9±1.2	58.1±0.8
8	42.1±0.7	42.2±0.4	44.6±2.1	41.1±1.3	60.7±1.3	62.03±0.4
9	43.5±0.5	44.3±0.3	51.1±0.6	43.4±0.4	65.3±0.9	64.6±0.47
10	44.7±1.1	46.2±0.7	53.8±1.3	44.8±1	68.2±0.8	67.31±1.7
11	47.4±1.0	50.2±1.7	57±0.4	54±1.1	70.2±0.8	71.7±1.1
12	54±0.05	55.6±2.2	58.2±0.5	56.8±3	75.4±0.7	77.1±1.8

Time (hrs)	F7	F8	F9	F10	F11	F12
0.5	14.52±0.6	14.94±0.6	15.6±0.1	14.55±1.4	16.88±0.9	13.85±1.2
1	25.14±1.4	24.49±2.0	27.7±0.7	27.57±0.8	25.4±1.8	27.3±0.9
2	32.6±3	31.93±3.0	39.2±0.5	38.31±1.1	37.5±1.5	35.5±2.2
3	37±4	37.26±2.0	57.08±1.6	57.4±1.2	53.74±1.3	41.8±1.5
4	44.41±1.8	43.93±3.6	66±1.7	62.4±1.4	58.75±0.9	55.09±0.8
5	48.4±1.0	47.35±2.8	65.57±0.5	66.16±0.7	63.4±1.4	65.25±0.8
6	53.4±2.5	53.85±2.8	67.9±1.0	69.49±2.0	66.9±1.3	67.08±1.7
7	55.97±3.1	55.98±2.5	72±2.6	73.64±2.4	72.4±2.0	73.8±1.5
8	59.3±2.3	60.67±1.4	76.46±0.3	77.5±1.4	76.9±1.8	76.7±1.2
9	63.11±3.1	65.45±0.6	82.3±0.6	82.37±0.7	81.87±1.7	80.6±1.3
10	64.97±2.8	67.1±1.0	86.4±0.8	86.48±0.9	87.2±0.2	87±0.2
11	69.02±3.27	68.8±1.4	90.2±1.0	91.78±3.1	94.25±2.1	92.67±2.0
12	75.4±0.1	75.4±0.7	95.87±0.5	96.7±1.4	99.9±1.2	95.5±0.9

All the values are expressed as mean ± S.D. n=3

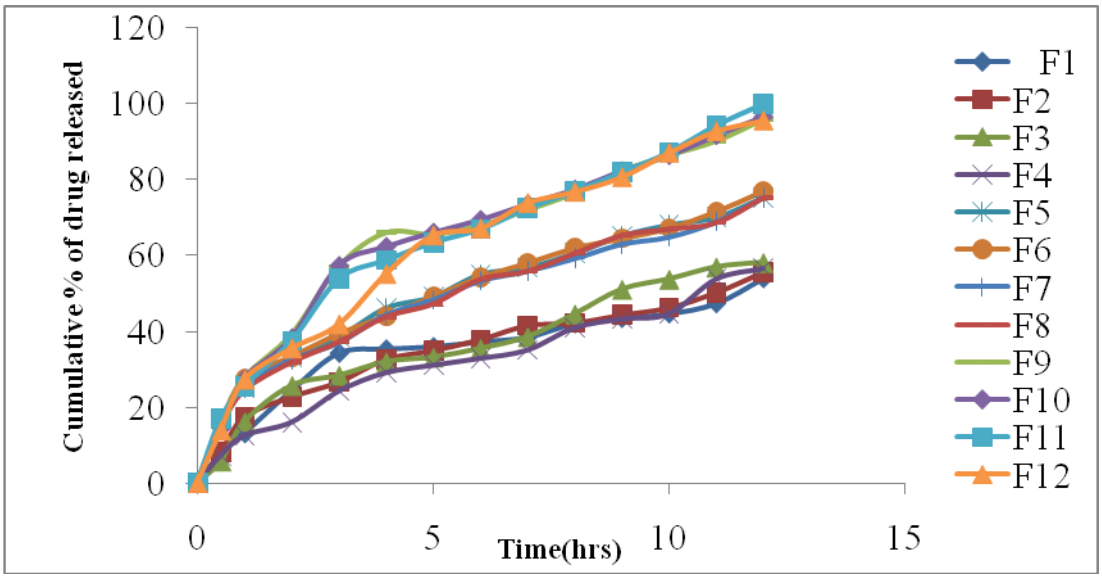


Fig 3. Cumulative % of drug released from all the formulations

Comparison of the optimized formulation (F11) with marketed formulation

The *in vitro* drug release of optimized formulation F11 was compared with that of the marketed film-coated tablets (BOSENTAS) containing 62.5mg of Bosentan Monohydrate per tablet. The comparative *in vitro* release profiles are shown in "Fig.4". The marketed formulation released 91% of the drug within one hour whereas the 99.9% drug was released for a period of 12hrs in case of the optimized formulation F11. This shows that the drug release was controlled from the optimized formulation F11 for 12 hrs which is because of slow release and increased gastrointestinal retention of the prepared tablets.

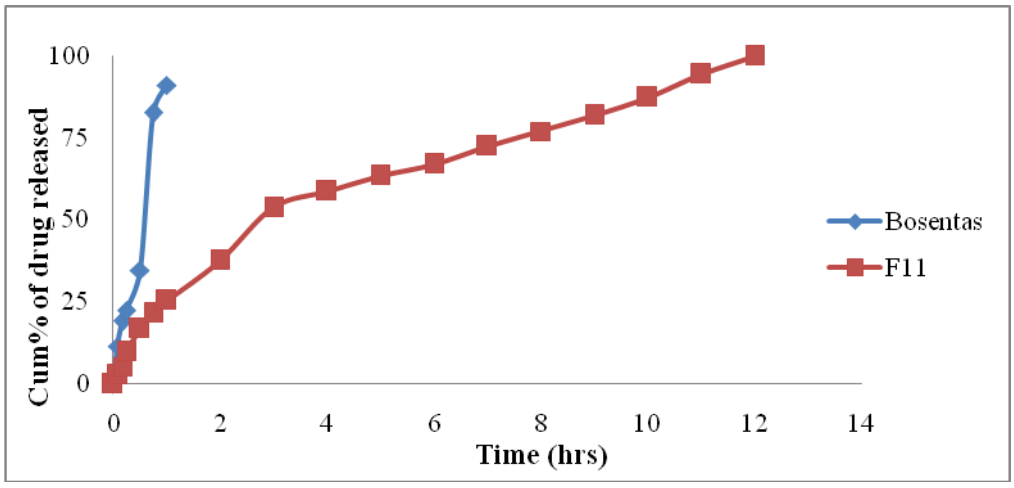


Fig 4. Comparison of dissolution profiles of marketed product and formulation F11

Drug-Excipient Compatibility studies

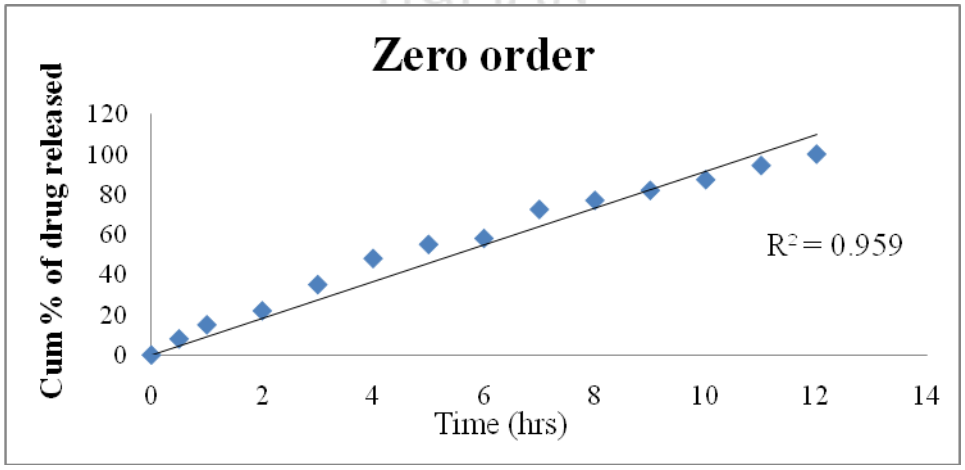
Fourier transform infrared spectroscopy (FTIR)

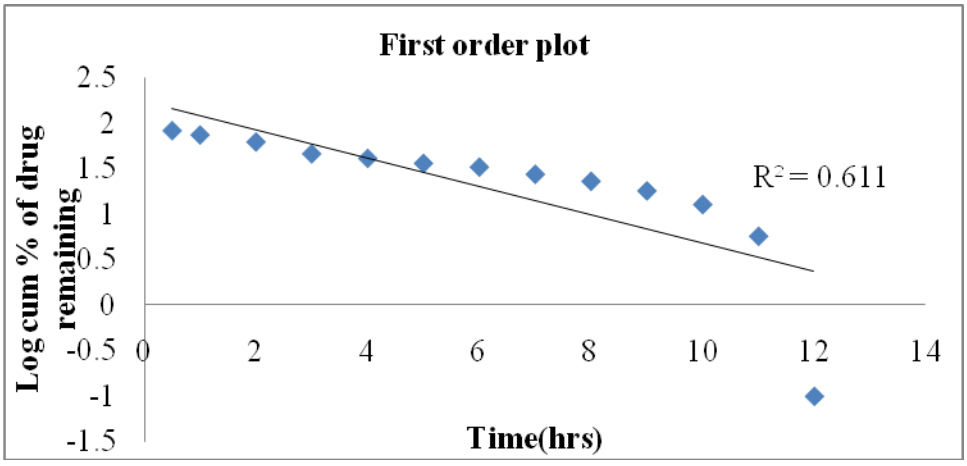
FTIR analysis revealed that there was no interaction between the drug and the polymers. The FTIR spectra of the pure drug and formulation indicated that the characteristic peaks due to pure Bosentan monohydrate have appeared in tablets and the positions of characteristic peaks of Bosentanwere not altered after their successful transformation into tablets, suggesting the absence of interactions between the drug and other components of the formulation indicated the stability of drug during formulation process.

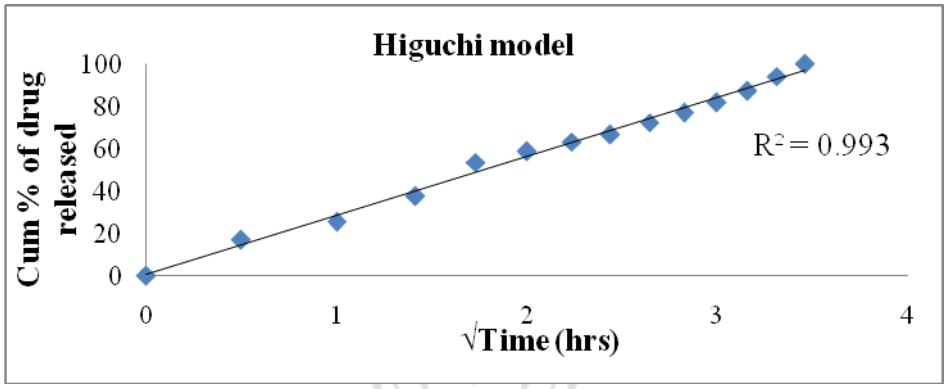
Phenomenon of Drug Release Kinetics

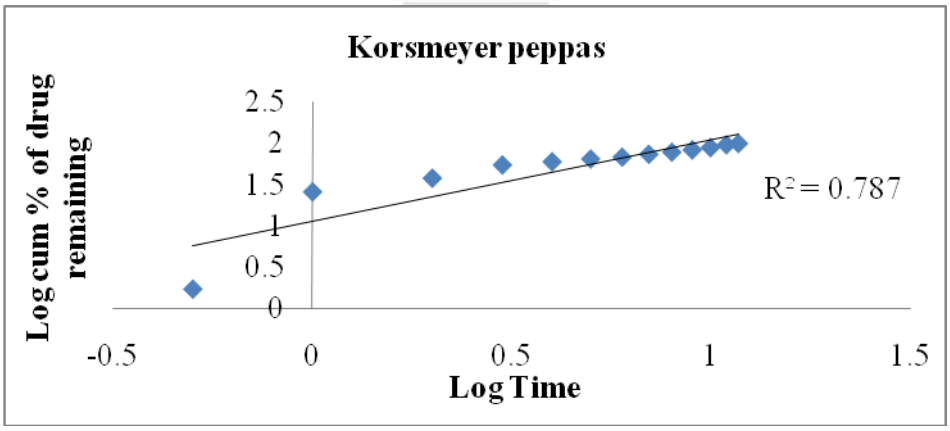
The optimized formulation F11 was subjected to a graphical representation to assess the kinetics of drug release. The release of drug was observed to follow the Zero order release kinetics. The initial burst effect was observed as per Zero order kinetics. Hence the drug release was mainly found to be concentration dependent. Hence it can be concluded that diffusion is the mechanism of drug released.

Release kinetics of optimized formulation F11









STABILITY STUDY:

Table 5: Post compression parameters after stability studies

Time	Disintegration	Hardness	Floating time
After 1 month	393.17±0.5	4.73±0.22	15±0.18
After 2 months	390.15±2.41	4.21±0.24	14±0.88
After 3 months	288.5±1.02	4.33±1.2	14±1.22

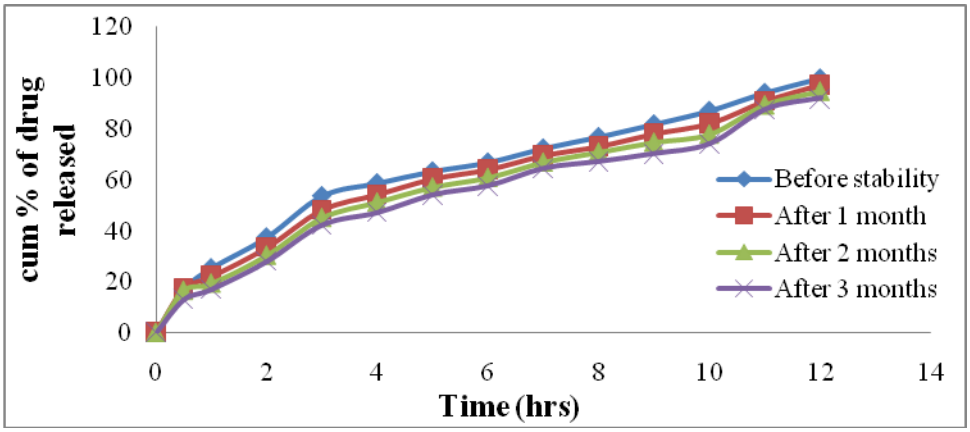


Fig 5. Drug release after stability

CONCLUSION:

From the present study, the following conclusions can be drawn:

- The controlled release raft tablets of Bosentan monohydrate were formulated and evaluated by direct compression method using different polymers.
- All the formulations have fulfilled the official limit for physicochemical parameters like weight variation, hardness, friability and drug content uniformity.
- IR spectra indicated the absence of probable chemical interaction between the drug and polymers used in different proportions.
- *In vitro* dissolution studies showed that 2:1:1 proportion is the best formulation to increase controlled effect due to the optimized polymer and pectin concentration.
- The optimized formulation F11 gave the best *in vitro* release of 99.9±1.2 in 12 hrs in 0.1N HCl. The release of drug followed fickian diffusion mechanism.

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