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The Utilization of Oil Entrapped Floating Alginate Beads in a Gastroretentive Delivery System is Intended to Improve the Bioavailbility of Telmisartan Incorporating Principles of Bioinformatics

Polaki Gauthami[1,*], Nansri Saha[2]

Abstract

Oil entrapped floating calcium alginate beads of Telmisartan were successfully prepared using sodium alginate as polymer and two different oil phases of mineral oil and olive oil by emulsion gelation method. The FT-IR spectra of final optimized formulation confirms no drug- polymer incompatibility. The floating time of beads was found to be more than 12 hrs suggesting that the method used for prepration was effective. The floating time of optimized formulation was within 6 minutes and floating time significantly increased as the amount of oil was increased in each formulation. The mean particle size of beads was in range from (1.204 mm to 2.0072 mm) depending upon the type of polymer used. The particle size increased significantly as the amount of polymer was increased in each preparation. The %Entrapment efficiency of beads ranging from41.14%–85.79% increased in concentration of polymer leads to increase in entrapment efficiency. The best formulation of oil entrapped floating calcium alginate beads of Telmisartan for mineral oil was found to be F5 98.03% and for Olive oil oil was found to be F7 96.7%, drug release in 12 hrs. The release kinetics of the optimized Telmisartan loaded oil entrapped beads showed that it follows Higuchi release kinetics. The release of the drug from the dosage form is carried out by diffusion and follows Korsmeyer peppas kinetics and the n value is greater than 0.5 indicating non-Fickian release. The floating beads have been employed to make a sustained release of the drug in the stomach to enhance bioavailability and to decrease dose dumping and hence overcome its side effects. The developed formulation shows an alternative to the conventional dosage form for the treatment of Telmisartan, a nonsedating antihistamine H1 blocker used for seasonal allergic rhinitis and chronic idiopathic urticaria has limited absorption in the upper small intestine with poor oral bioavailability. Hence finally it was concluded that the prepared oil entrapped floating sodium alginate beads of Telmisartan may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency and improved oral bioavailability.

***Author for Correspondence**
Polaki Gauthami
E-mail: gouthamipolaki@gmail.com

[1]Student, Department of Pharmaceutics, SSJ College of Pharmacy, Hyderabad, Telangana, India
[2]Associate Professor, Department of Pharmaceutics, SSJ College of Pharmacy, Hyderabad, Telangana, India

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Keywords: Gastroretentive Delivery System, Floating Alginate Beads Bioavailability, Telimisartan

INTRODUCTION:

Oral formulations have earned a significant place among the various dosage forms developed so far for human administration. In most of the cases, the

conventional oral delivery systems show limited bioavailability because of fast gastric-emptying time among many other reasons involved [1, 2]. However, the recent technological development has resulted to many novel pharmaceutical products, mainly the controlled release drug delivery systems to overcome this problem. Gastro-retentive drug delivery system (GRDDS) is one such example where the attribute like gastric retention time coupled with the drug release for extended time has significantly improved patient compliance. Some inherent limitations of the conventional oral drug delivery systems have ignited the interest to this new delivery system. Fast gastric emptying associated with conventional oral medications leads to a bioavailability issue for many drug molecules (e.g. pranlukast hydrate, metformin HCl, baclofen, etc.), of which the main principal site of absorption is the stomach or the proximal part of the small intestine, or have the absorption issue in the distal part of the intestine [3, 4, 5]. Solubility can also be improved by prolonging the gastric retention of drugs that are less soluble in an elevated pH environment of the intestine. There are many drugs (e.g. captopril, metronidazole, ranitidine HCl, etc.) that are prone to degradation in the colonic area, [6]. To attain required therapeutic activity, recurrent dosing is needed for the drugs with short half-lives as they have the tendency of getting eliminated quickly from the systemic circulation. However, an oral sustained-controlled release formulation with additional gastric retention property can avoid these limitations by releasing the drug slowly in the stomach along with maintaining an effective drug concentration in the systemic circulation for an extended period of time [7]. Apart from the systemic action, GRDDS has proved to be effective locally to treat gastric and duodenal ulcers, including esophagitis, by eradicating the deeply buried Helicobacter pylori from the submucosal tissue of the stomach, [8, 9, 10]. The history of GRDDS formulations dates back to almost three decades [11]. The basic fabrication techniques, including their in vitro characterizations, are also well established. Even in recent times, quite a few reviews have been published on GRDDS [12, 13, 14, 15, 16, 17, 18]. These reviews are more focused on the formulation aspects or in vitro characterization studies done by various researchers or overall GRDDS. The industrial aspects covering physicochemical, biopharmaceutical and regulatory considerations of GRDDS have been reviewed by Pawar et al. [19].

To develop and characterize the oil entrapped floating alginate beads of Telmisartan for enhancing oral bioavailability. Telmisartan (Telmisartan), a nonsedating antihistamine H1 blocker used for seasonal allergic rhinitis and chronic idiopathic urticaria has limited absorption in the upper small intestine with poor oral bioavailability of approximately 33%. Therefore, Telmisartan is considered as a potential drug candidate for GRDDS.

In a previous study effervescent floating GRDDS of Telmisartan was designed for the first time as an alternative to conventional tablets, in an attempt to control drug release over 24 h. But the effervescent tablets having several disadvantages Floating drug delivery systems are among the several approaches that have been developed in order to increase the gastric residence time of dosage forms. etc., A wide variety of newer drug delivery system being designed and evaluated in the recent years to overcome the limitations of conventional drug therapy Oral drug administration is preferred generally over the other routes of administration to treat chronic diseases. However, many potential orally active drug candidates are suffering with low oral bioavailability caused by low solubility, low permeability and high first pass metabolism or combinations thereof. In that case the delivery system would serve dual purpose; the released drug would act locally in the lumen as well as systemically after absorption of drug through the basolateral membrane.

MATERIALS AND METHODS

Experiment Protocol

Stage-I

Preparation of Dissolution Medium Acid Buffer (pH1.2)

Place 50 ml of 0.02 M Pottasium chloride in a 200 mlvolumetric flask, add the specified volume of 0.2M hydrochloric acid and make up the volume with water as seen in Table 1 and Table 2

Table 1. List of materials used in formulation.

S.N.	Name of the material	Manufacturer/Supplier	Applications
1.	Telmisartan	Aurobindo Pharmaceuticals, Hyderabad, India	Active ingredient
2.	Sodium alginate	Nice chemicals Pvt.Ltd., India	Hydrophilic Polymer
3.	Liquid paraffin	Nice chemicals Pvt.Ltd., India	Oil Phase
4.	Olive oil	Qualigens Fine chemicals, India	Oil phase

Table 2. Iformulation table for telmisartan loaded oil entapped floating alginate beads.

Formulation code	Telmisartan (mg)	Sodium alginate %w/w	Liquid paraffin %v/v	Olive oil %v/v
F1	120	2%	10	-
F2	120	2%	15	-
F3	120	2%	20	-
F4	120	4%	10	-
F5	120	4%	15	-
F6	120	4%	20	-
F7	120	2%	-	10
F8	120	2%	-	15
F9	120	2%	-	20
F10	120	4%	-	10
F11	120	4%	-	15

Preparation of 0.2M Pottasium chloride

- Dissolve 14.911gm of potassium chloride in water and dilute to 1000ml with water

Preparation of 0.2M Sulphuric acid

- Dilute 17ml of concentrated hydrochloric acid in to 1000ml with water

Determination of λmax by UV Spectrophotometry

Dissolving 100 mg of Telmisartan.HCL in methanol to made the stock solution in 100 ml volumetric flask. From this stock pipette out 10 ml of solution and make upto 100 ml with methanol. From this solution different dilutions were prepared in pH1.2 acid buffer to achieve working standard then the absorbance was observed at 220 nm in UV-Visible spectrophotometer.

Development of Standard Calibration Curve

The graph was plotted between absorbance v/s concentrations to obtain the standard calibration curve

Drug-Polymer Compatibility Studies

Fourier Transform Infrared Spectrocopic(FT-IR) Studies

Drug sample is identified by FTIR. Sample drug Spectrum of FTIR compared with standard drug FTIR spectrum. FTIR spectral analysis of pure drug and polymers will carried out and observation is made whether changes in the chemical constitution of drug after combining it with the polymers occurred. The samples are crushed with KBr to get pellets by applying pressure on 600 Kg/cm2 and scanned with the IR instrument from 400- 4000cm-1. Infra-Red spectroscopy is one of the most powerful analytical techniques to recognize functional groups of a drug.

Stage-II

Development of floating alginate beads

Formulation of TELMISARTAN Sodium Alginate Beads with Mineral Oil

Emulsion gelation method was selected for the preparation oil entrapped beads. Emulsion gelation method is simpler than the ones used so far for the preparation of other floating dosage form**.**

Telmisartan HCL loaded *sodium alginate* beads were prepared by the emulsion–gelation method. In this method, the sodium alginate solution was prepared in water in different ratio **(***2%, 4%). Mineral oil (Liquid paraffin)* in concentrations *(10%, 15% and 20% v/v),* was then added to the polymer solution to make mixtures. To ensure emulsion stabilization, the mixtures were homogenized at 10,000 rpm using a homogenizer for 10 min. Telmisartan HCl was then dispersed in the formed emulsion. The bubble-free emulsion was extruded; using a 23G syringe needle into 100 ml gently agitated (5%) calcium chloride solution at room temperature. The emulsion gel beads were allowed to stand in the solution for 20 min before being separated and washed with distilled water. The beads were air-dried at room temperature and stored in a air tight container.

Formulation of TELMISARTAN Sodium Alginate Beads with Olive Oil

In this method, the *sodium alginate* solution was prepared in water in different ratio *(2%,4%). Olive oil* in concentrations *(10%, 15% and 20% v/v),* was then added to the polymer solution to make mixtures. To ensure emulsion stabilization, the mixtures were homogenized at 10,000 rpm using a homogenizer for 10 min. Telmisartan HCl was then dispersed in the formed emulsion. The bubble-free emulsion was extruded; using a 23G syringe needle into 100 ml gently agitated (5%) calcium chloride solution at room temperature. The emulsion gel beads were allowed to stand in the solution for 20 min before being separated and washed with distilled water. The beads were air-dried at room temperature and stored in a air tight container

Stage-III

Evaluation of oil entrapped floating beads

Measurement of Bead Size

The diameter of beads was determined by screw gauge. For this purpose, 20 dried beads were randomly selected from each batch and the mean diameter was calculated . The least count of screw gauge was 0.005 mm. The color and shape of dried beads of each batch was visually observed.

%Entrapment Efficiency

50 mg of beads were weighed and crushed in a mortar pestle and the crushed material was dissolved in few ml of methanol balance volume is made up with acid buffer pH(1.2) washings of mortar. This solution was shaken with the help of Rotary flask shaking machine for 5 hrs and then kept for 24 hrs. Then it was filtered by using whatman filter paper. The filtrate was assayed by spectrophotometricaly at 220 nm. The drug content and the entrapment efficiency were determined.

The % drug entrapment efficiency of each bead formulation was calculated using the following equation

Actual amount of drug (AQ)/Theoretical amount of drug (TQ) X 100

Morphological Study by Scanning Electron Microscope (SEM)

Morphological examination of the surface and internal structure of the optimized bead was performed by using scanning electron microscope (SEM). The samples placed on the stubs using a carbon adhesive tape, coated with gold palladium alloy using a fine coat ion sputter (JEOL, fine coat ion sputter JFC-1100) and then surface topography was analyzed under scanning electron microscope (JSM 6100 JEOL, Tokyo, Japan) operated at an acceleration voltage of 15 Kv as seen in Table 3 and Table 4.

Swelling Index Study

Beads were studied for swelling characteristics. Sample from drug- loaded beads were taken, weighed and placed in a USP dissolution apparatus typeII. The beads was placed in a jar containing 900 ml of HCl solution (pH 1.2) maintained at 37±0.5ºC. After 12 hours the beads were removed from their respective swelling media and weighed after drying the water on the surface of the beads using filter paper.

$$\text{Swelling Index} = \frac{\text{Final wt.of Beads} - \text{Initial wt.of Beads}}{\text{Initial wt.of Beads} \times 100}$$

In vitro Buoyancy Study

The buoyancy ability of beads was determined using USP type II (Paddle type) dissolution apparatus.The drug loaded beads were placed in the dissolution vessel containing 900 ml of acid buffer (pH 1.2) maintained at 37±0.5 ◦C for 12 h and the paddles were rotated at 50 rpm. The floating ability of the beads was measured by visual observation. The time taken for the beads to float at the surface of the dissolution medium (known as floating lag time) and duration of floating (buoyancy) for each batch of beads were noted**.**

In Vitro Drug Release Studies

The dissolution rate of the prepared beads was studied using USP rotating paddle dissolution apparatus II. Known weight of beads containing equivalent amount of 120 mg of Telmisartan HCL was placed in the dissolution medium containing 900 ml of pH 1.2 acid buffer. The temperature was maintained at 37+0.5°C with an rpm of 50. 5 ml of sample was withdrawn at specified time intervals and replaced with fresh dissolution medium. The samples were filtered with 0.45 μm Whatmann membrane filter and the quantity of the drug released was determined using UV spectrophotometer at 220 nm. FT-IR spectral analysis as seen in Table 5.

The pure drug, sodium alginate, drug-loaded optimized beads from each mineral oil, olive oil entrapped were analyzed by FTIR spectroscopy to assess the drug-excipients compatibility. Samples were reduced to powder and analyzed as KBr pellets by using a Fourier transform infrared (FTIR) spectroscope. The pellet was placed in the sample holder and spectral scanning was taken in the wavelength region between 4000 and 600 cm^{-1} at a resolution of 4 cm^{-1} with scan speed of 1 cm/s *(Hriday Bera et al., 2015)*

Analysis of Invitro Release Studies Kinetics

To analyze the *in vitro* release data various kinetic models were used to describe the release kinetics. The zero order rate Equation (1) describes the systems where the drug release rate is independent of its concentration. The first order Equation (2) describes the release from system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion Equation (3). The Hixson-Crowell cube root law Equation (4) describes the release from systems where there is a change in surface area and diameter of particles.

$$C = kot \quad (1)$$

Where, K0 is zero-order rate constant expressed in units of concentration/time and t is the time.

$$LogC = LogCo - kt/2.303 \quad (2)$$

Where, C0 is the initial concentration of drug and K is first order constant.

$$Q = Kt^{1/2} \quad (3)$$

Where, K is the constant reflecting the design variables of the system.

$$Q0^{1/3} - Qt^{1/3} = KHC\ t \quad (4)$$

Where, Qt is the amount of drug released in time t, Q0 is the initial amount of the drug in tablet and KHC is the rate constant for Hixson-Crowell rate equation. The following plots were made:

Zero order release kinetics: Cumulative% drug release vs. time.
First order release kinetics: Log cumulative of % drug remaining vs. time.
Higuchi Model: Cumulative % drug release vs. square root of time.
Korsmeyer-Peppas Model: Log cumulative % drug release vs. log time.

Hixson-Crowell cube-root Model: Cube root of drug % remaining in matrix vs. Time

RESULT AND DISSCUSSION

Preformulation Studies

Color, Odour and Taste

White to off-white coloured fine powder. It is odorless and has a slight characteristic taste observed by descriptive terminology

Standard Calibration Curve for Telmisartan HCL

Table 3. Calibration data for telmisartan. HCL

Concentration in µg/ml	Absorbance
5	0.1661
10	0.3918
15	0.5737
20	0.7925
25	0.9734
30	1.2068
35	1.3719
40	1.6078
45	1.7098
50	2.0000

Prepared calibration curve of drug Telmisartan by using acid buffer (pH1.2). The drug absorbance was measured at 220 nm using UV double beam spectrophotometer. The linearity of the absorbance as seen in Figure 1.

was found to be from the concentration between 5-50mcg/ml (*Regression value =0.999) and its obeys beer's lambertz law.*

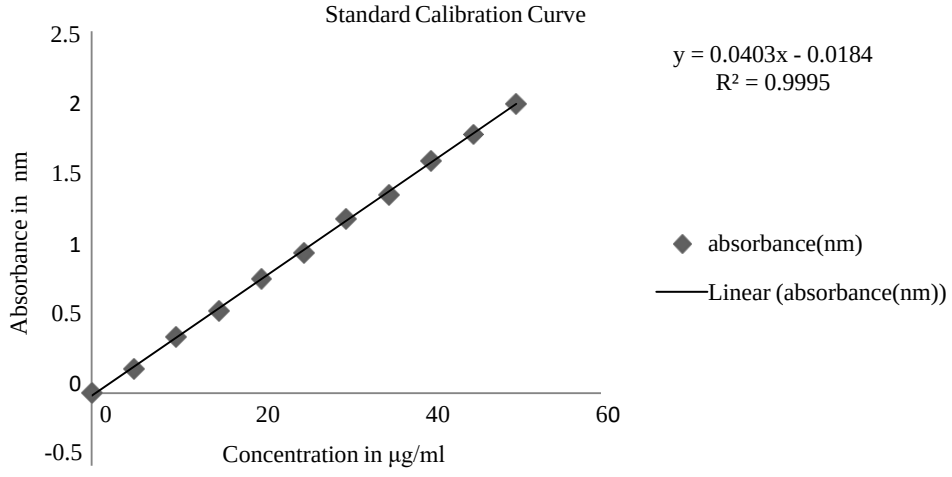

Figure 1. Standard Calibration Curve for Telmisartan.

Hydrochloride

Drug-Polymer Compatibility Studies

The characteristic peaks of standard Telmisartan were reported in the IR spectrum which indicated that the obtained sample was pure and when compared indicated there was no interaction between the

drug and polymers as the characteristic peaks of drug were reported in the physical mixture. This confirms the compatibility of the drug with the polymer used for the formulation of oil entrapped gastro retentive beads as depicted as seen in Figure 2.

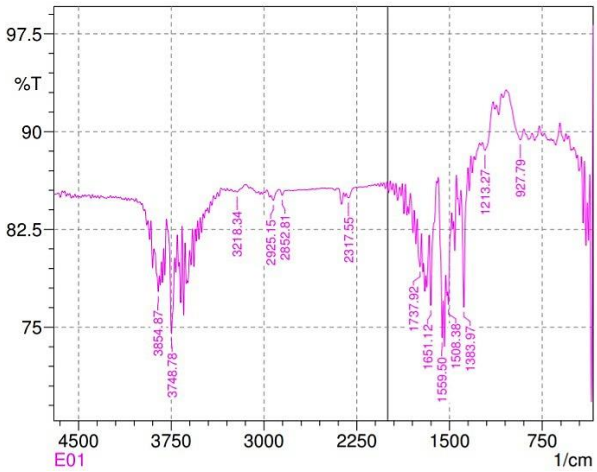

Figure 2. FT-IR Spectra for telmisartan.

Table 4. IR spectral interpretation of telmisartan.

Wavenumber (cm^{-1})	Type of vibration
1737.920	C=O Strectching
3218.000	O-H Stretching
1383.970	C-O Sretching

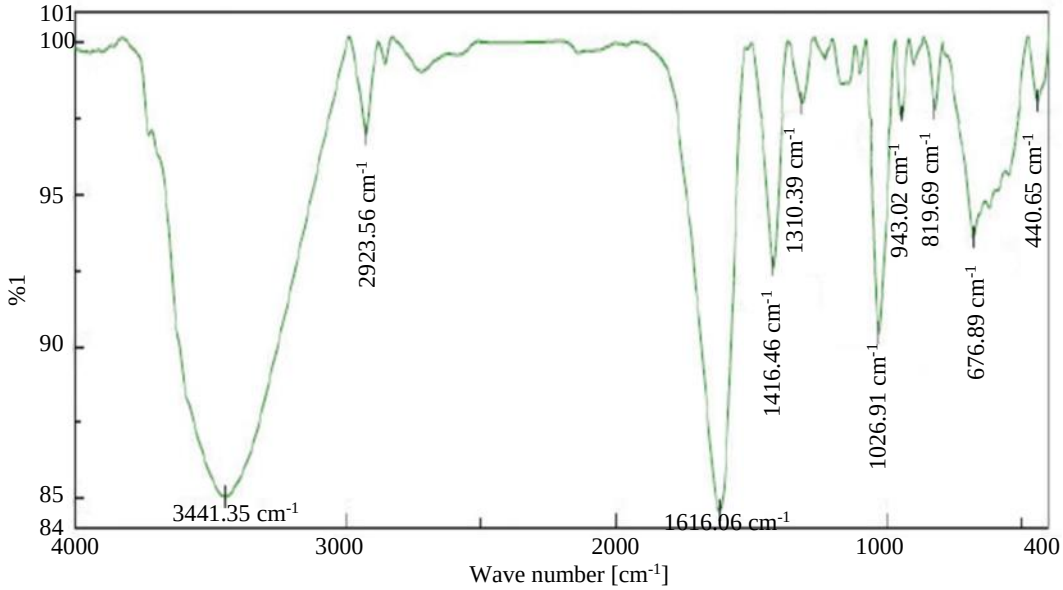

Figure 3. T-IR Spectra for telmisartan with sodium alginate.

Table 5. IR Interpretation of telmisartan with sodium alginate.

Wavenumber (cm^{-1})	Type of vibration
1616.060	C=O Strectching
34441.350	O-H Stretching
2923.500	C-HSretching
1559.500	Nitro group

Formulation of Oil Entrapped Beads

Spherical gel beads were formed instantaneously when emulsion was dropped into calcium chloride solutions. Gelation occurred due to intermolecular cross-linking between the divalent calcium ions and the negatively charged carboxyl groups of sodium alginate as seen in Figure 3.

Figure 4. Photograph of formulated beads.

Sodium alginate promoted the emulsification of the mixture of water and oil phases during homogenization and the resulting oil droplets were dispersed in calcium crosslinked network of the formulation as seen in Figure 4.

Evaluation of Formulated Beads

Measurement of Bead Size

The prepared beads were almost spherical .The mean surface diameter of all 9 formulations was between 1.204 mm and 2.1 mm tabulated in Table 1.The size of the bead was found to be increased as the concentration of polymer and oil was increased.

The diameter of the beads increased significantly as polymer concentration increased; this could be attributed to the increase in the microviscosity of the polymeric dispersion, eventually leading to the formation of larger beads. Larger size beads were also formed as the concentration of calcium chloride increased as seen in Figure 5. This may be due to excess calcium ions causing possibly all the crosslinking sites in the polymer to be fully utilized and resulting in larger but weaker and flexible gel beads as seen in Table 6

Table 6. Bead size in mean diameter.

Batch code	Mean diameter±S.D (mm) (n=20)
F1	1.2±0.039
F2	1.55±0.01
F3	1.69±0.024
F4	1.63±0.0105
F5	1.75±0.031
F6	2.0072±0.026
F7	1.204±0.03
F8	1.56±0.015
F9	1.67±0.012
F10	1.71±0.0107
F11	1.85±034
F12	2.1±0.031

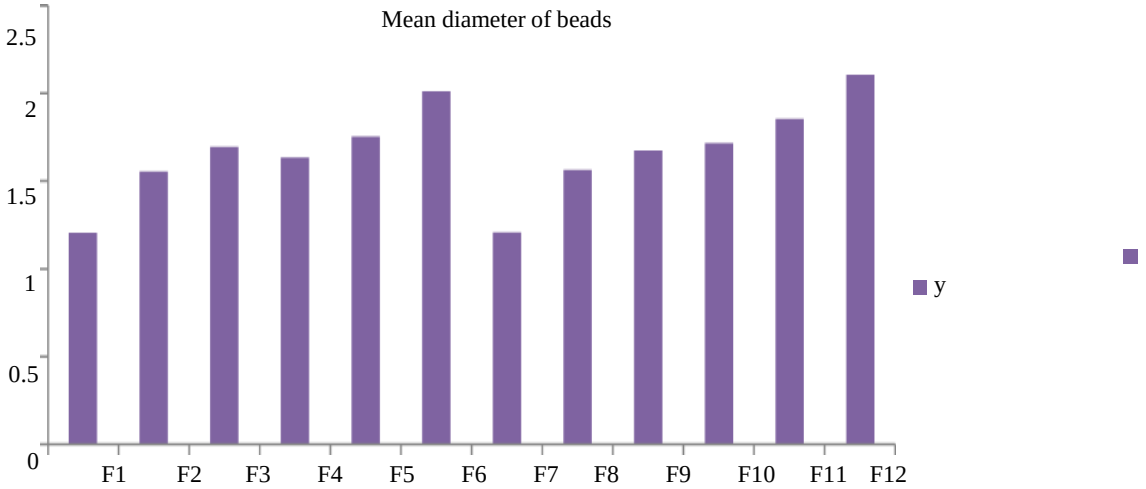

Figure 5. Mean diameter of all formulated beads(F1-F12).

%Entrapment Efficiency

All beads were evaluated for actual drug content and entrapment efficiency. Results revealed that entrapment efficiency was found to be minimum for F2 (41.16%) and maximum for F10(85.8%). Drug entrapment efficiency were found to be increasing with respect to increase in concentration of polymer.as seen in Figure 6.

The encapsulation efficiency of the beads influence as polymer concentration increased due to the availability of excess polymer which ensured that the drug was optimally entrapped. On the other hand, encapsulation efficiency decreased with increase in calcium chloride concentration because excess Ca2+ would have the effect of weakening the polymer gel structure and strength, thus leaving it more porous and limiting its capacity to trap the drug as seen in Table 7 and Table 8.

Table 7. %Entrapment effieiency of beads.

Batch code	%Entrapment Efficiency ±S.D (n=3)
F1	44.57±0.025
F2	41.16±0.044
F3	54.49±0.023
F4	63.95±0.045
F5	74.48±0.012
F6	66.66±0.02
F7	57.03±0.035
F8	59.39±0.06
F9	70.32±0.033
F10	85.76±0.021
F11	48.6±0.05

Morphological Study by Scanning Electron Microscope (SEM)

Surface morphology of the prepared floating beads was examined by SEM. The SEM images was taken for the optimized formulation F5. The beads were spherical with a uniform texture and smooth surface. The external surface was slightly rough surface/shrinkage which could be due to drying Samples were taken from optimized formulations and operating conditions for SEM observation. The oil entrapped Calcium alginate structure formed showed the sponge-like structure where the oil was entrapped. This sponge- like structure may correspond to the egg-box structure of calcium alginate

which was rigid and water insoluble. The pores of the oil-entrapped Cal. Alg. beads represented the oil droplets, and their size was influenced by concentration of oil. The morphology of the external and internal structure was identical. The surface of oil-entrapped cal. Alg. beads showed small pores containing oil droplets dispersed all over the structure. These are unique to the floating calcium alginate beads and enable floatation as seen in Figures 7–10**.**

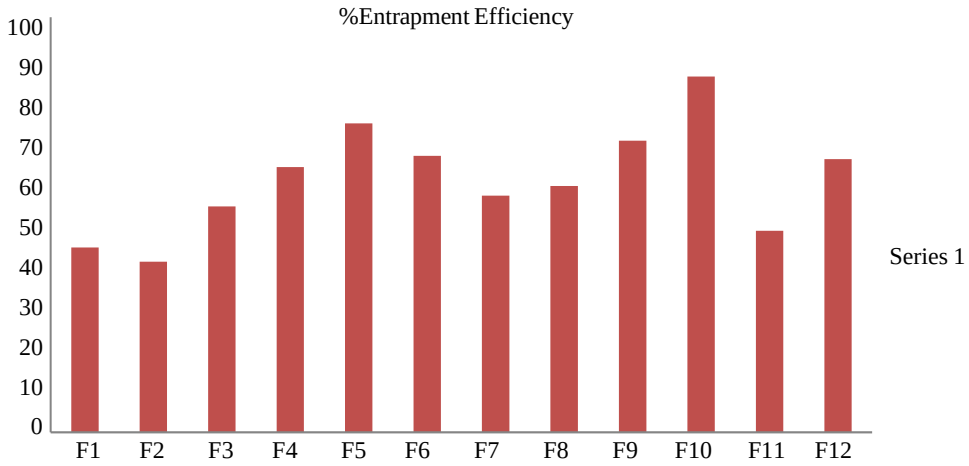

Figure 6. %Entrapment efficiency of F1-F12 formulations.

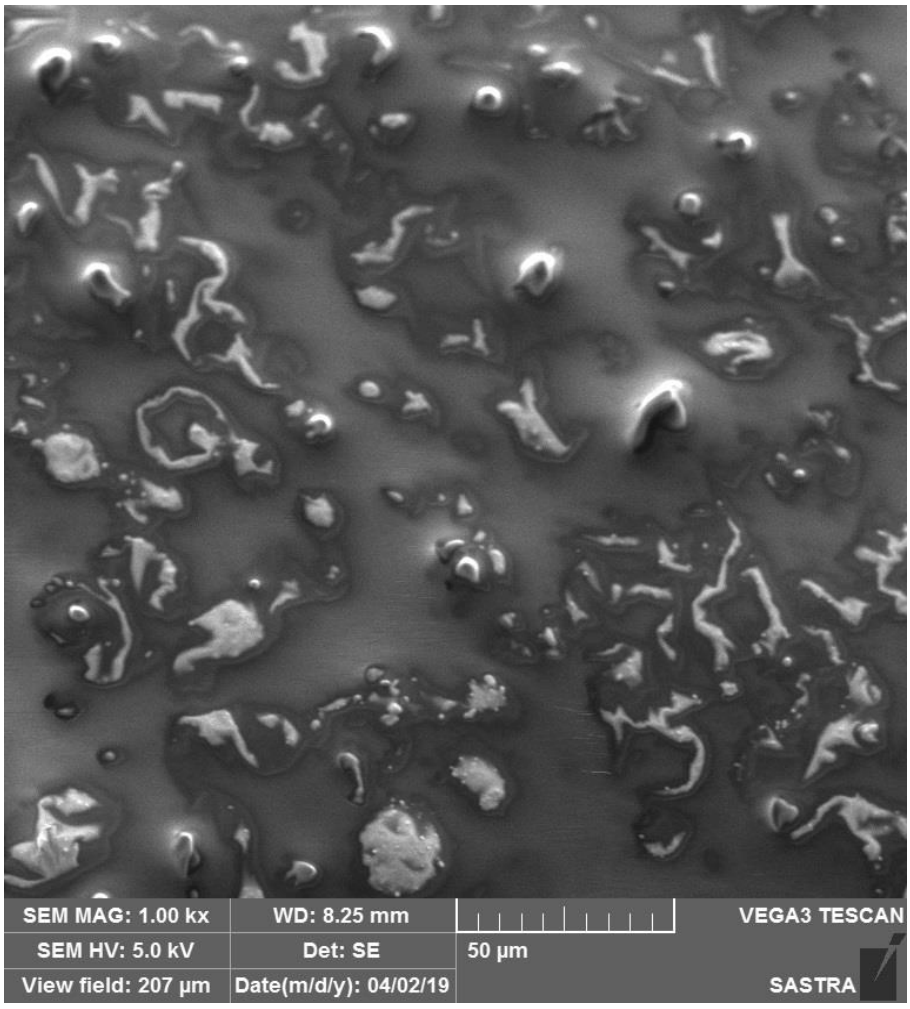

Figure 7. SEM photograph of optimized formulation (F5)-8.25 mm.

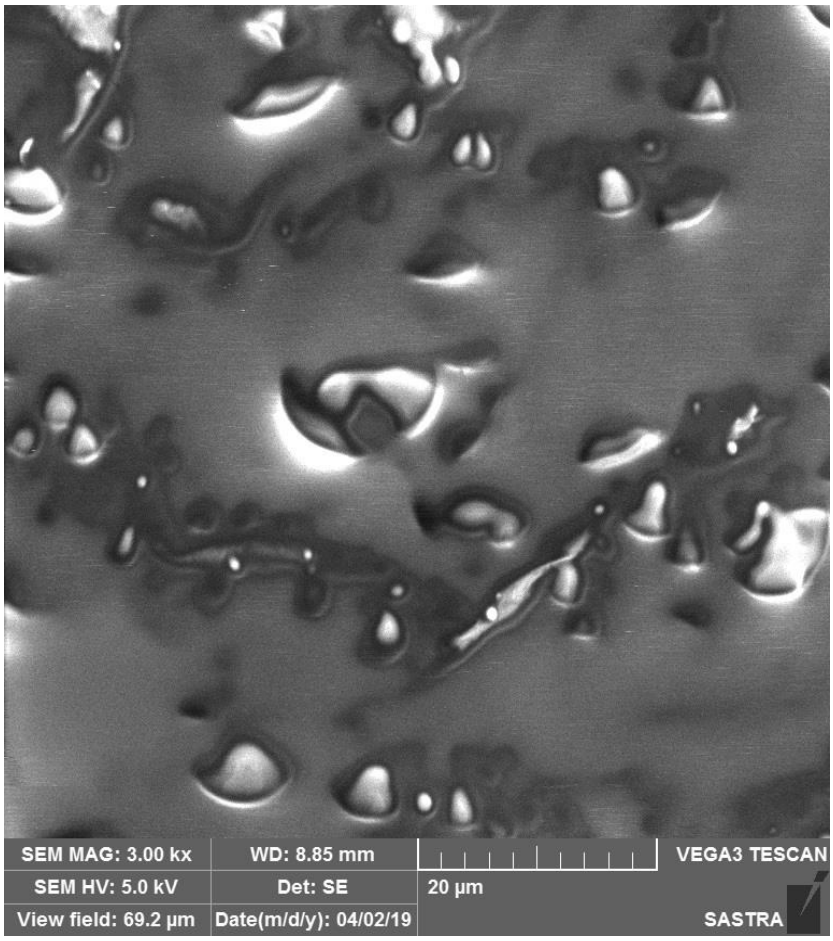

Figure 8. SEM photograph of optimized formulation (F5)-8.85 mm.

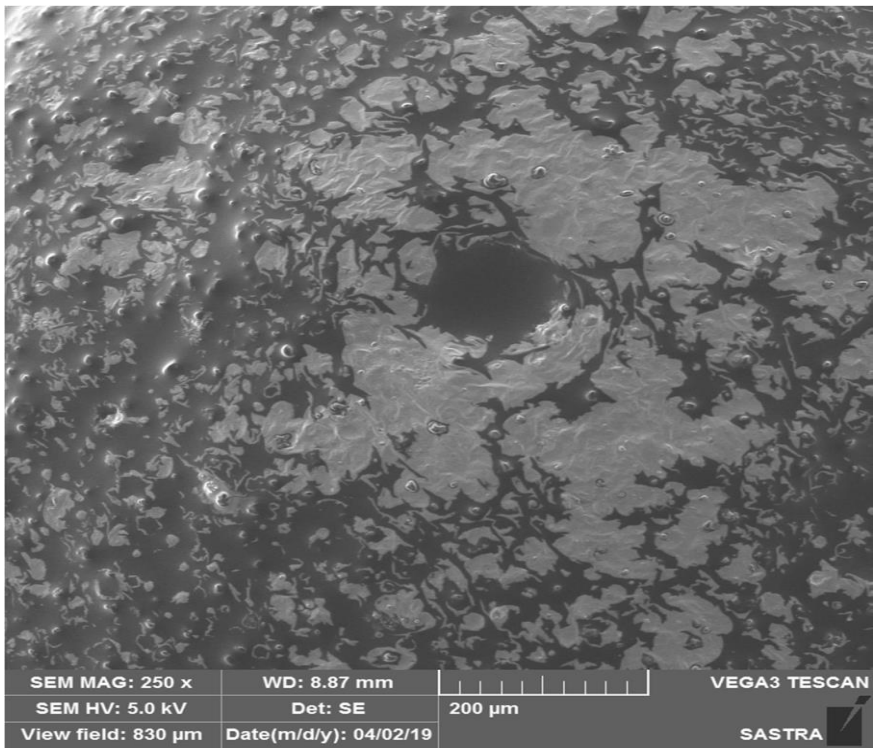

Figure 9. SEM photograph of optimized formulation (F5)-8.87 mm.

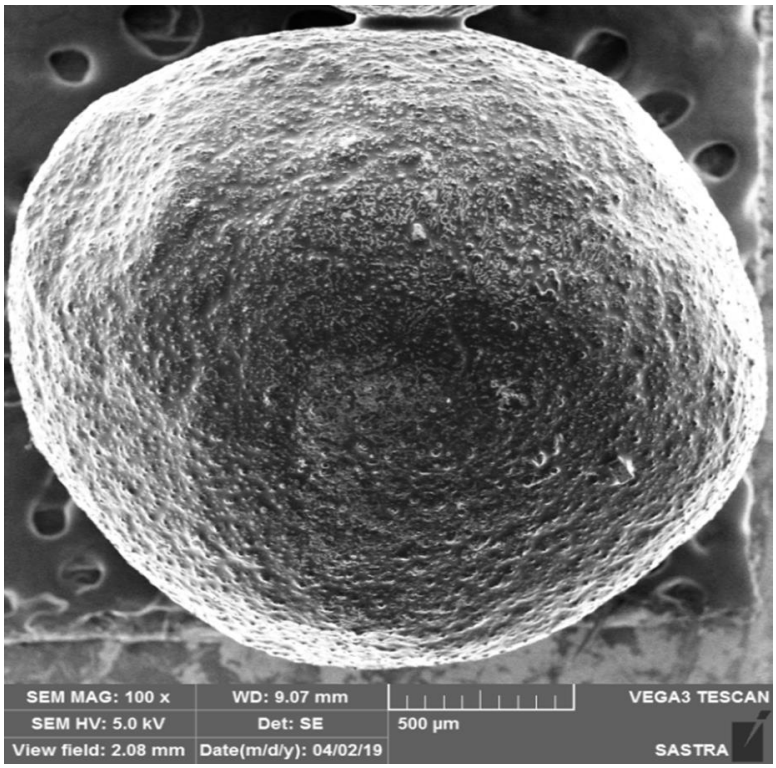

Figure 10. SEM photograph of optimized formulation (F5)-9.07 mm.

Swelling Index Study

The amount of polymer directly affected the solvent transfer rate thus, as the polymer concentration increased the swelling index also increased. In vitro swelling studies were carried in 0.1NHCL at 37°C and degree of swelling index for each was determined gravimetrically. Swelling index for all formulation increased as the concentration of polymer increased as seen in Table 9, 10, 11.

Table 8. Swelling index of beads

Batch code	Swelling index
F1	7.24
F2	7.16
F3	7.67
F4	10.77
F5	13.18
F6	13.00
F7	7.27
F8	6.30
F9	6.59
F10	11.97
F11	5.89
F12	7.10

In Vitro Buoyancy Study

Buoyancy is an important factor in sustained drug delivery to the gastric region. All the beads floated on simulated gastric fluid for up to 12 h. Increase in the calcium chloride content of the beads resulted in a decrease in floating lag time, due to increase in the porosity of the gel beads. Floating lag time also rose as the concentration of oil in the formulation increased and this can be attributed to flocculation of the oil globules which might also have coalesced to produce large droplets as seen in Figures 11–13.

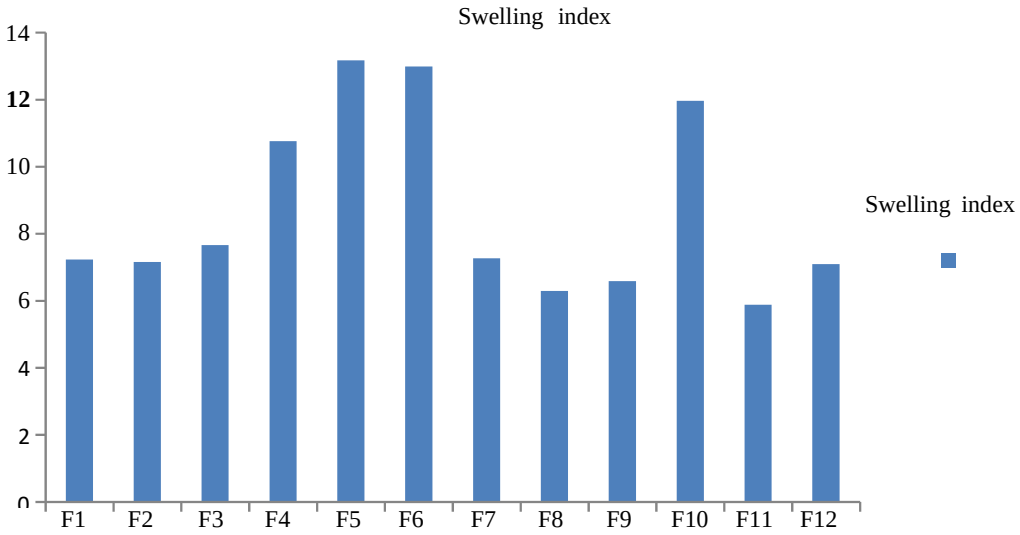

Figure 11. Swelling index of beads.

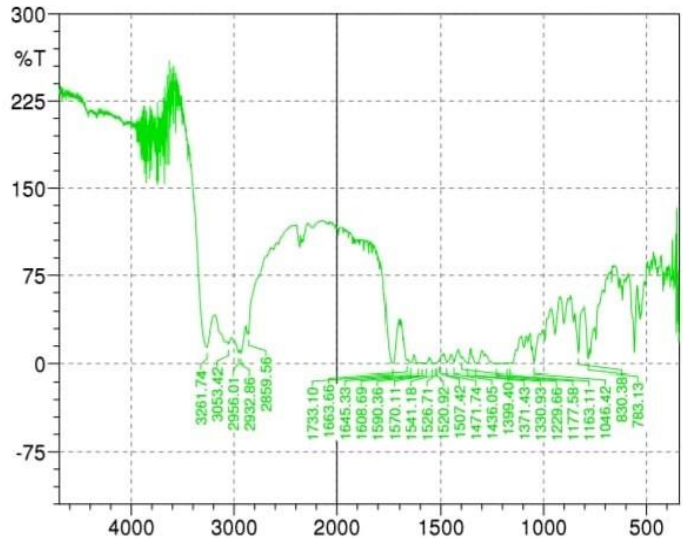

Figure 12. IR Spectrum of optimized bead formulation(F5) from mineral oil entrapped beads.

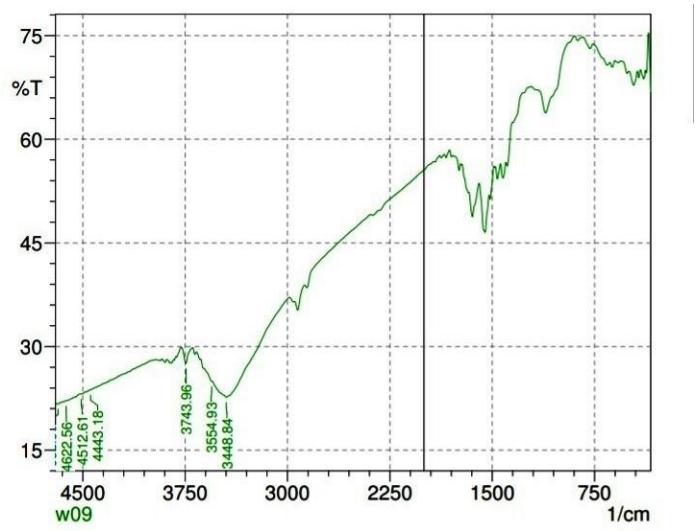

Figure 13. IR Spectrum of optimized bead formulation(F10) from Mineral oil entrapped beads.

Table 9. In vitro buoyancy of all formulations (F1-F12).

Batch code	Floating lag time in minutes	Floating time in hours
F1	41.000	>12
F2	32.000	>12
F3	10.000	>12
F4	12.000	>12
F5	6.000	>12
F6	4.000	>12
F7	45.000	>12
F8	15.000	>12
F9	10.000	>12
F10	3.000	>12
F11	8.000	>12
F12	7.000	>12

Table 10. Cumulative % drug release of formulation F1-F4.

Time in Hours	F1(%)	F2(%)	F3(%)	F4(%)
0	0	0	0	0
0.5	15.9	18	16.3	13.4
1	21.3	23.6	20.5	17.2
2	25.4	28.03	31.05	24.07
3	46.03	50.1	32.3	36.08
4	52.3	53.8	39.8	43.4
5	61.05	58.6	43.8	50.02
6	68.6	64.9	48.04	56.6
8	75.3	73.6	52.6	61.9
10	80.8	79.2	59.06	67.4

Table 11. Cumulative % drug release of formulation F5-F6.

Time in Hours	F5(%)	F6(%)	F7(%)	F8(%)
0	0	0	0	0
0.5	18.7	13.8	17.4	15.9
1	21.7	15.5	20.6	20.3
2	37	26.4	24.6	31.3
3	50.8	29.8	35.3	35.9
4	56.8	35.5	41.5	43.4
5	62.01	40	48.1	51.7
6	66.6	46.7	52.6	58.7
8	72.4	53.07	61.7	67.02
10	83.1	56.9	69.7	73.02
12	98.03	77.3	82.5	87.3

Table 12. Cumulative % drug release of formulation F9-F12.

Time in Hours	F9(%)	F10(%)	F11(%)	F12(%)
0	0	0	0	0
0.5	15.2	16.8	15.5	14.2
1	19.8	26	18.9	17.9
2	28.7	36.07	23.6	25.5
3	36.4	41.6	28.6	30.01
4	43.9	46.5	32.4	34.5
5	47.9	51.2	39.7	38.4
6	52.7	59.2	50.05	42.3
8	56.1	67.3	56	49.2
10	60.6	76.1	63.4	54.8
12	79.6	96.7	71	66.4

FT-IR spectral analysis

The FT-IR spectra study was performed optimized formulation F5, F10 showed no change in the finger print of pure drug spectra, thus confirming absence of drug and polymer interaction

In Vitro drug release studies

In vitro drug release from the floating beads of Telmisartan HCL (for Mineral oil and olive oil) was found to be from 66.40% to 98.03%. Among all formulation, F5 was found to be the best formulation for Mineral oil as its release 98.03%, F10 was found to be the best formulation for olive oil as its release 96.71% in a sustained manner with constant fashion over an extended period of time. Drug release pattern was affected by polymer concentration, ratio of polymer mixture and amount of oil. The results indicate that the drug release slows down with increasing polymer concentration. It can be explained that greater the amount of polymer, thicker the layer of polymer was formed around the drug particles and more effectively the polymer would hold the drug with itself. This had also been proved with the result of entrapment effieiency.

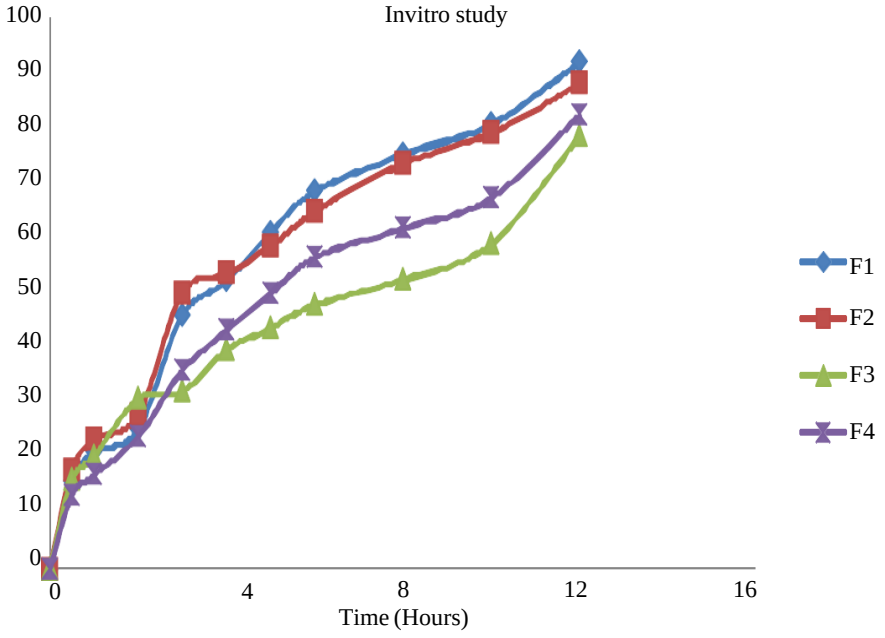

Figure 14. Cumulative % drug release of formulation F1-F4.

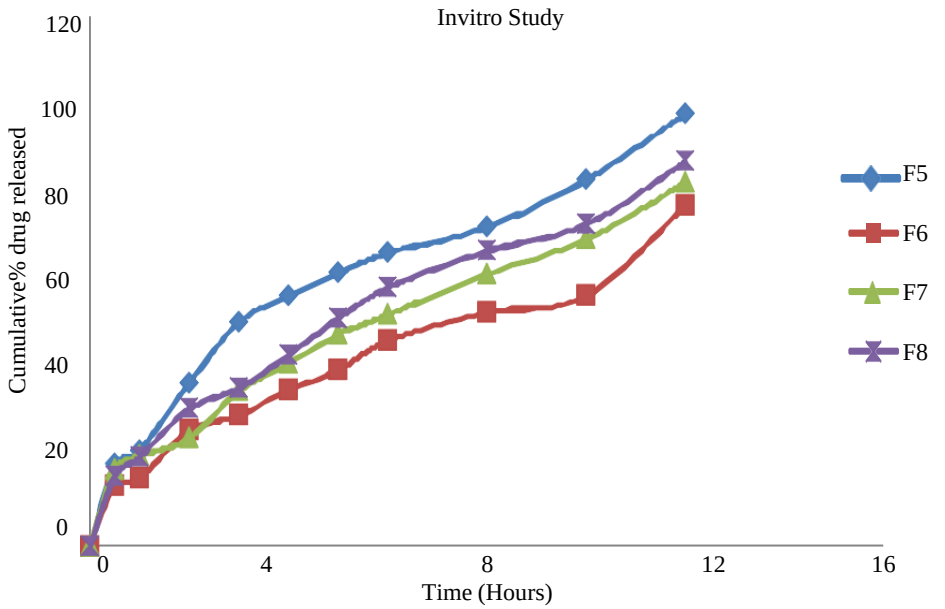

Figure 15. Cumulative % drug release of formulation F5-F8.

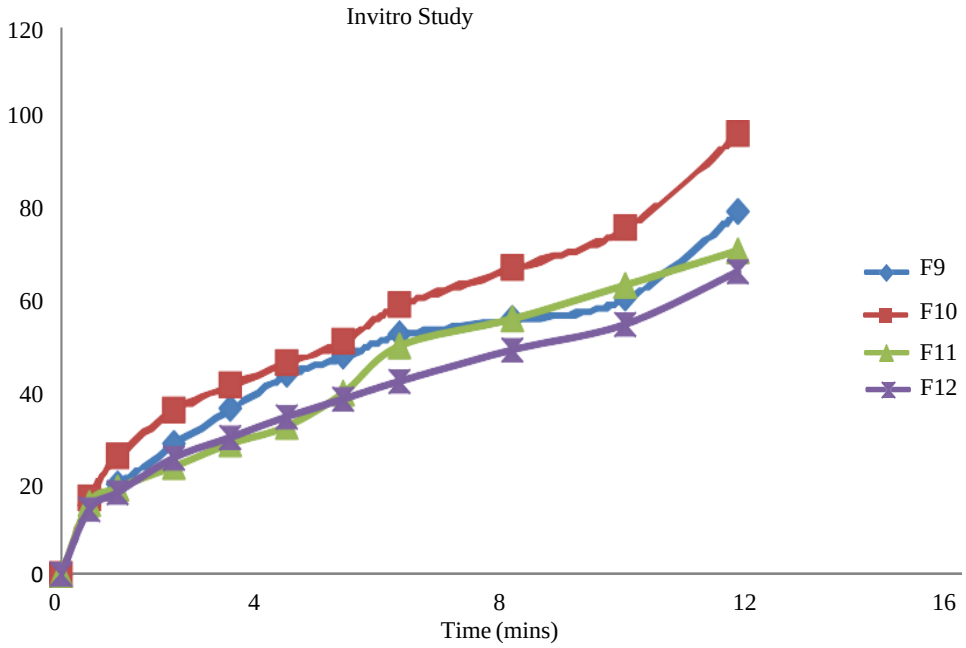

Figure 16. Cumulative % drug release of formulation F9-F12.

In Vitro Drug Release Kinetics

The in vitro release data was fitted into zero-order, first-order,Higuchi, Hixson–Crowell and Korsmeyer–Peppas models to estimate the release kinetics. In order to describe the kinetics of drug release from formulations, various equations were used, such as the zero-order rate equation, which describes the systems where the release rate is independent of the concentration of the dissolved species. The first-order equation describes the release from systems where dissolution rate is dependent on the concentration of the dissolving species. *In vitro* data were also fitted to Higuchi's square root model , which describes the release from systems where the solid drug is dispersed in an insoluble matrix, and the rate of drug release is related to the rate of drug diffusion. The results established that, in most cases, the drug release rate obeyed Higuchi kinetic model. The n value for all formulations is greater than 0.5 which indicated anomalous or non fickian diffusion as senen in Table 12 and Table 13.

Table 13. In vitro drug release kinetics of all formulations (F1-F12).

Batch code	Zero order	First order	Higuchi model	Kores-meyer and peppas model		Hixon-crowell model
	R2	***R2***	***R2***	***R2***	***n***	***R2***
F1	0.915	0.973	0.981	0.641	1.196	0.981
F2	0.897	0.984	0.984	0.601	1.142	0.974
F3	0.924	0.919	0.97	0.581	1.046	0.938
F4	0.94	0.969	0.985	0.661	1.17	0.975
F5	0.911	0.831	0.989	0.603	1.158	0.938
F6	0.95	0.931	0.969	0.648	1.107	0.952
F7	0.956	0.972	0.985	0.623	1.113	0.983
F8	0.95	0.962	0.99	0.625	1.139	0.981
F9	0.913	0.933	0.981	0.601	1.085	0.943
F10	0.944	0.799	0.979	0.577	1.101	0.908
F11	0.955	0.987	0.977	0.629	1.084	0.983
F12	0.939	0.975	0.99	0.603	1.038	0.97

The *in-vitro* drug release of formulations showed the highest regression coefficient values for higuchi model(0.969-0.99)), thus indicating absolute correlation between the two variables for the Higuchi model as seen in figure 14,15,1. All formulations followed Higuchi's equation proving that the release is by diffusion mechanism. The values of release exponent (n) were calculated from Korsmeyer and Peppas equation and the 'n' values was determine to be(1.038-1.196) indicating Anomalous (non-fickian) diffusion.

SUMMARY AND CONCLUSION

- Oil entrapped floating calcium alginate beads of Telmisartan were successfully prepared using sodium alginate as polymer and two different oil phases of mineral oil and olive oil by emulsion gelation method.
- The FT-IR spectra of final optimized formulation confirms no drug- polymer incompatibility.
- The floating time of beads was found to be more than 12 hrs suggesting that the method used for prepration was effective. The floating time of optimized formulation was within 6 minutes and floating time significantly increased as the amount of oil was increased in each formulation.
- The mean particle size of beads was in range from (1.204mm to 2.0072mm) depending upon the type of polymer used. The particle size increased significantly as the amount of polymer was increased in each preparation.
- The %Entrapment efficiency of beads ranging from41.14%-85.79% increased in concentration of polymer leads to increase in entrapment efficiency
- The best formulation of oil entrapped floating calcium alginate beads of Telmisartan for mineral oil was found to be F5 98.03% and for Olive oil oil was found to be F7 96.7 %, drug release in 12 hrs.
- The release kinetics of the optimized Telmisartan loaded oil entrapped beads showed that it follows Higuchi release kinetics. The release of the drug from the dosage form is carried out by diffusion and follows Korsmeyer peppas kinetics and the n value is greater than 0.5 indicating non-Fickian release.
- The floating beads have been employed to make a sustained release of the drug in the stomach to enhance bioavailability and to decrease dose dumping and hence overcome its side effects.
- The developed formulation shows an alternative to the conventional dosage form for the treatment of Telmisartan, a nonsedating antihistamine H1 blocker used for seasonal allergic rhinitis and chronic idiopathic urticaria has limited absorption in the upper small intestine with poor oral bioavailability .

- Hence finally it was concluded that the prepared oil entrapped floating sodium alginate beads of Telmisartan may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency and improved oral bioavailability.

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