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Design, Development, Evaluation and Optimization of Microballoons of Telmisartan

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Research Article

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Abstract: In present study an attempt was made to prepare microballoons of Telmisartan by emulsion solvent diffusion technique for sustained delivery by using polymers like Ethyl cellulose to extend the drug release for about 12 hours in the upper GIT, which may result in enhanced absorption and there by improved bioavailability. Formulation optimization of Telmisartan loaded microballoons was carried out by using different concentration of Polyvinyl alcohol (PVA) and Ethyl cellulose. Total 9 batches were formulated. All 9 batches were evaluated for entrapment efficiency (EE) and buoyancy. Among all batches DP4 shows maximum entrapment efficiency (EE) and buoyancy and was considered as optimized formulation. DP4 batch was further used for process optimization. The process optimization was carried out at three different stirring speeds i.e. 1300, 1500 and 1700 rpm for three different stirring time period i.e. 1hr, 2hr and 3 hr and another 9 batches were formulated. Out of all the batches DP13 showed the spherical shape of microballoons without formation of flakes. Optimized batch DP13 was evaluated for Zeta Potential, Particle Size Distribution which show -41.8mV and 1.344 µm particle size, SEM, XRD Analysis. Batch DP13 was charged for stability and were placed in glass vials container and stored at ICH storage condition (2°C - 4°C Refrigeration condition , 30 ± 2°C / 60% ± 5% RH , 40 ± 2°C / 75% ± 5% RH) for a period of 30 days. The samples were analyzed for physical appearance, buoyancy and for the drug release after 30 days. After 1 months samples were withdrawn and microballoons showed no change in physical appearances, buoyancy and drug release, which indicate that the microballoons were stable.

Keywords: Telmisartan, Microballoons, Emulsion solvent diffusion technique, Buoyancy, Entrapment Efficiency.

INTRODUCTION

Microballoons are gastro-retentive drug delivery systems based on non-effervescent approach. Microballoons are in strict sense, spherical empty particles. These microballoons are characteristically free flowing powders consisting of proteins or synthetic polymers, ideally having a size less than 200 micrometer. Gastro-retentive Microballoons are low-density systems that have sufficient buoyancy to float over gastric contents and remain in stomach for prolonged period. The drug is released slowly at desired rate resulting in increased gastric retention with reduced fluctuations in plasma drug concentration. Microballoons to improve patient compliance by decreasing dosing frequency, better therapeutic effect of short half-life drugs can be achieved. Enhanced absorption of drugs which solubilise only in stomach, Gastric retention time is increased because of buoyancy [1-3]. Telmisartan is an angiotensin II receptor blocker that shows high affinity for the angiotensin II receptor type1 (AT_1), with a binding affinity 3000 times greater for AT_1 than AT_2. The AT_1 receptor is located predominantly in the vascular and myocardial tissue, brain, kidney and adrenal glomerulose which secretes aldosterone. Telmisartan blocks the aldosterone secreting effects of angiotensin-II, and is used for controlling mild to moderate hypertension. Drug that shows solubility in upper gastro intestinal track at higher pH condition results in low and incomplete release of drug from the formulation. Drug release and absorption of these type of drug may improved by formulating such type of dosage form that remains in stomach for longer period of time thus drug absorption in acidic pH for longer period of time and therapeutic effect of drug is for longer period of time. Telmisartan shows higher absorption at upper part of gastro intestinal track was selected for the study [4].

MATERIALS AND METHOD

Telmisartan was obtained from Aarti Drugs Ltd, Mumbai. Ethyl cellulose, Tween 80, Poly Vinyl Alcohol (PVA), Methanol, Dichlor methane (DCM) were procured from Sulab Laboratory, Vadodara.

Method of Preparation of Microballoons

Emulsion Solvent Diffusion Technique is a new approach to prepare microballoons. The drug to polymer ratio used to prepare the different formulations were 1:3, 1:5 and 1:7. In this technique, the drug and polymer was dissolved in organic solvent [i.e. methanol: DCM (3: 3). Then, the dispersion solution was added drop-by-drop into 0.5% PVA solution containing 0.3% Tween 80. Resultant emulsion was stirred at 1400 rpm using a propeller-type agitator for 2 hour. The microballoons were separated by filteration, washed with water and dried at room temperature in a desiccator for 24 hr [5, 6].

CHARACTERIZATION OF MICROBALLOONS [7-10]

Fourier Transform Infrared Spectroscopy (FTIR)

The microballoons were subjected to Fourier Transform Inferred Spectroscopy (FTIR) studies using (Shimadzu 8400 s). The potassium bromide (KBr) disk method was used for preparation of sample. The spectrum was compared with the infrared spectra of plain drug and polymer and checked for the drug-polymer interaction.

Percentage Practical Yield

The prepared microballoons were collected and weighed. The measured weight was devided by total amount of all non-volatile components which were used for preparation of microballoons.

$$\%\ \textbf{Practical Yield} = \frac{\textbf{Weight of dried microballoons}}{\textbf{Weight of solid used (excipients + drug)}} \times \mathbf{100}$$

Drug Entrapment Efficiency

Separation of free drug: Analysis of Telmisartan from microballoons was done by separating free drug from the microballoons dispersion. The separation was done by filtration (Whatmann filter paper) of microballoons. Then, the microballoons and filtrate were separated out.

Indirect method

In this method, analysis of drug from microballoons was done by appropriately diluting filtrate in distilled water and absorbance was taken at 296 nm against distilled water as a blank on UV-Visible Spectrophotometer. To find out % entrapment following equation was used.

$$\%\ \textbf{EE} = \frac{\textbf{Weight of total drug} - \textbf{Weight of free drug in filtrate}}{\textbf{Weight of total drug}}$$

Drug Loading Efficiency

% Drug loading was calculated using following equation

$$\%\textbf{Drug Loading efficiency} = \frac{\textbf{Weight of Drug loaded in microballoons}}{\textbf{Total weight of powdered microballoons}} \times \mathbf{100}$$

Scanning Electron Microscopy

SEM is an instrument that produces largely magnified image by using electrons instead of light to form an image. The morphology of optimized formulation of Telmisartan loaded microballoons was determined using scanning electron microscopy (SEM).

X-ray diffraction study

Powder X-ray diffraction (XRD) was performed for both pure drug and optimized formulation of Telmisartan loaded microballoons to investigate the effect of polymerization on crystallinity of the drug.

Measurement of particle size and zeta potential

Zeta potential of a microballoons reflects the electric potential of particles and is used to characterize the surface charge properties and to determine whether the charged particle is encapsulated within the centre or adsorbed on to the surface of microballoons. The Particle size and Zeta potential of microballoons was recorded using Zetasizer. The optimized formulation was subjected to particle size and zeta potential analysis.

In-Vitro Buoyancy Studies

50mg of microballoons were placed in simulated gastric fluid (pH 1.2, 100ml) containing 0.02 w/v % tween 20. The mixture was stirred at 100 rpm in magnetic stirrer. After 6 hr, the floating and the settled portion of microballoons were recovered separately by filtration. The microballoons were dried and weighed. Both the fractions of microballoons

were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$\textbf{Buoyancy (\%)} = W_F / (W_F + W_S) * 100$$

Where, W_F and W_S are the weights of floating and settled microballoons respectively.

In Vitro Diffusion Studies

In-vitro drug diffusion of optimized formulation of Telmisartan loaded microballoons in present research work was carried out by Dialysis Bag diffusion method. A 4–5 cm long portion of the dialysis tubing was made into a dialysis sac by folding and tying up one end of the tubing with thread. It was then filled up with simulated gastric fluid (pH 1.2) containing 0.02 w/v % tween 20 and examined for the leaks. The sac was then emptied and 100 mg of the microballoons was accurately transferred into sacs, which served as the donor compartments. The sacs were once again examined for leak and then suspended in the glass beakers containing 200 ml simulated gastric fluid (pH 1.2) containing 0.02 w/v % tween 20, which become the receptor compartment, and maintained at 37± 0.5°C at a rotation speed of 100 rpm. At predetermined time intervals, 5 ml samples were withdrawn from the receptor compartment and analyzed spectrophotometrically. Fresh simulated gastric fluid was used to replenish the receptor compartment at each time point.

Release Kinetics [11]

In order to understand the mechanism and kinetics of drug release, the results of the *in vitro* drug release study were fitted with various kinetic equation a namely zero order (%release vs. t), first order (log% unreleased vs. t), and higuchi matrix (%release vs. square root of time). In order to define model which will represent a better fit for the formulation, drug release data further analyzed by korsmeyer peppas equation, Mt/M is the fraction of drug released at time t, k is the kinetic constant and n is the diffusional exponent, a measure of the primary mechanism of drug release. R^2 values were calculated for the linear curves obtained by regression analysis of the above plots.

Stability Study [12]

The stability study was carried out for optimized formulation of Telmisartan loaded microballoons as per ICH guidelines. The microballoons of the best formulation were placed in glass vials and stored at ICH storage condition (2°C - 4°C Refrigeration condition , 30± 2°C / 60% ± 5% RH and 40 ± 2°C / 75% ± 5% RH) for a period of 30 days. The samples were analyzed for physical appearance, %buoyancy and for the drug release after 30 days.

RESULTS AND DISCUSSION

Microballoons of Telmisartan in different ratios were designed and prepared by Emulsion solvent diffusion technique. Drug-polymer compatibility studies were carried out using FTIR spectroscopy to establish any possible interaction of Telmisartan with the polymer used in the formulation. Thus results indicate that the characteristic absorption peak due to pure Telmisartan have appeared in the formulated microspheres without any significant change in their position indicating no chemical interaction between Telmisartan and polymers (Fig-1-4). In every formulation the floating time was found out to be greater than 24 hr.

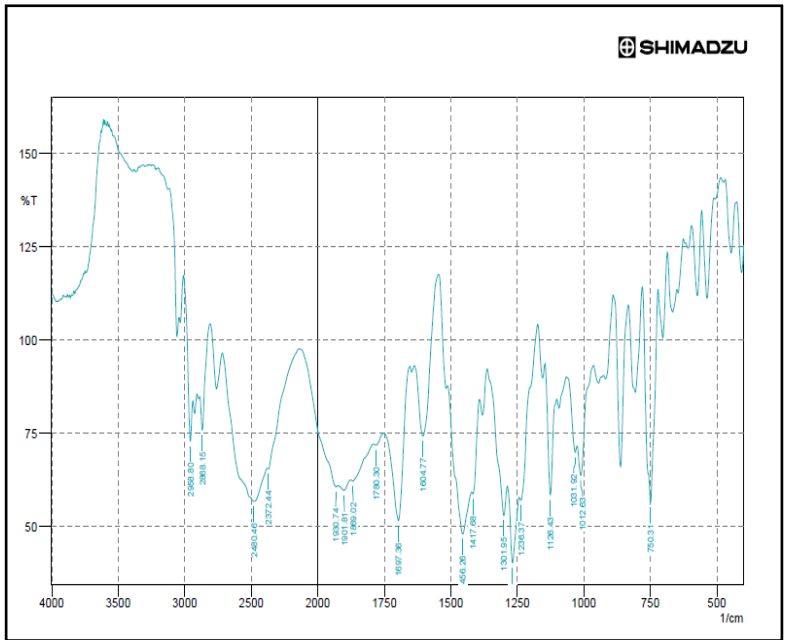

Fig-1: FTIR Spectra of Telmisartan

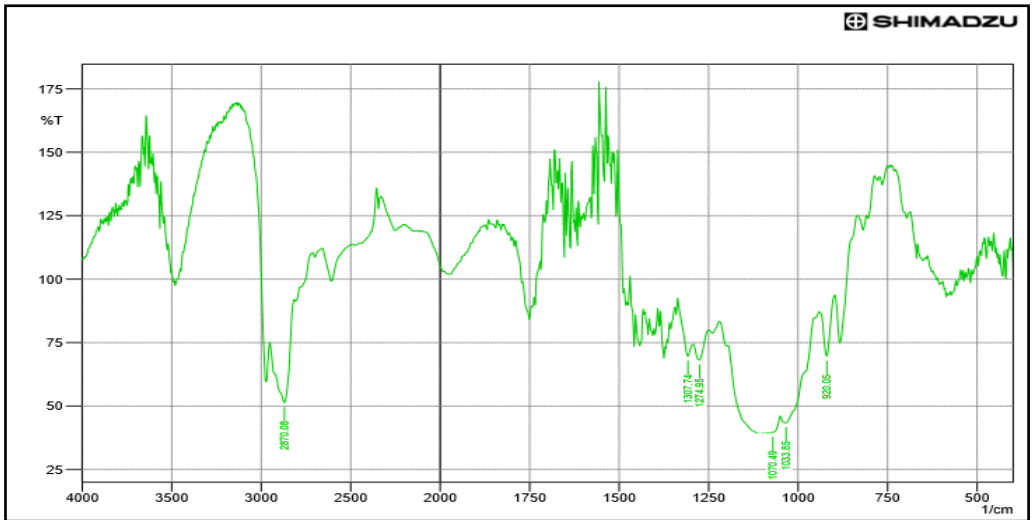

Fig-2: FTIR Spectra of Ethyl cellulose

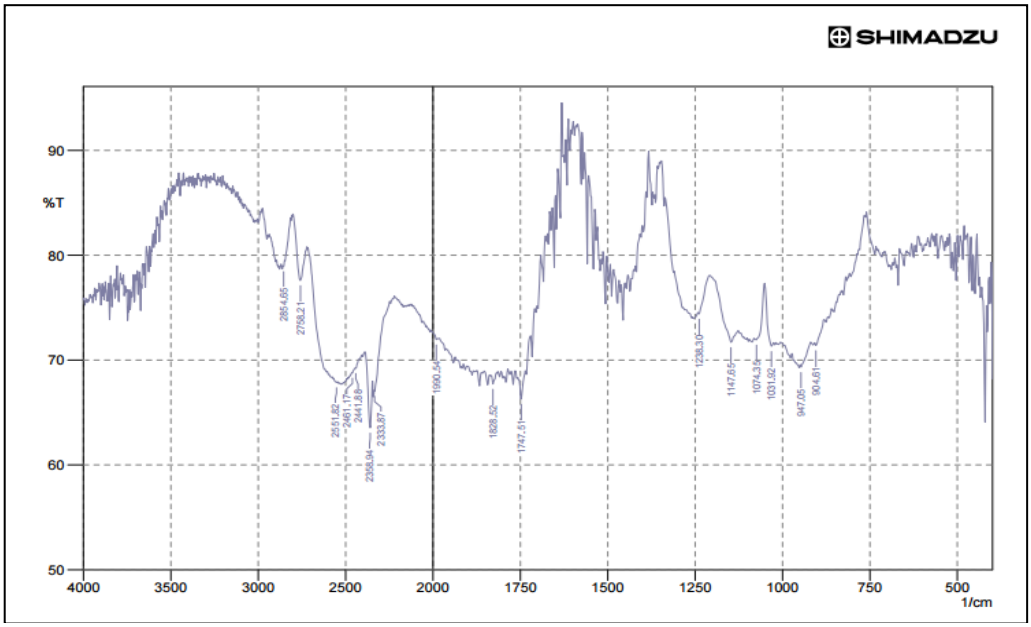

Fig-3: FTIR Spectra of PVA

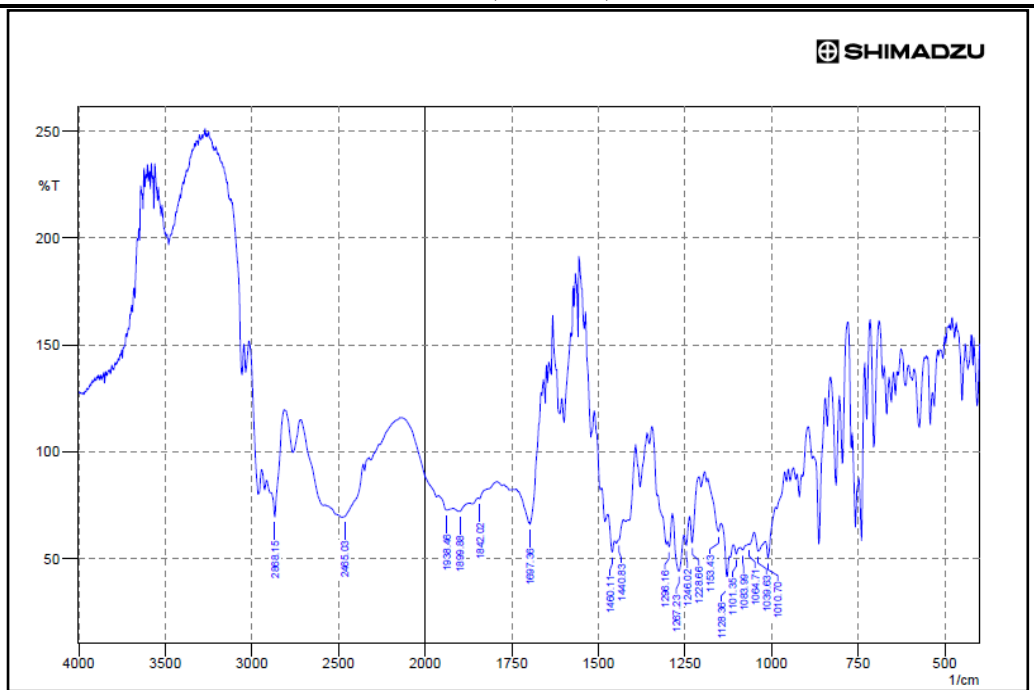

Fig-4: FTIR Spectra of Telmisartan + ethyl cellulose

Formulation Optimization

Formulation optimization has been done by 3^2 factorial designs

Table-1: Factors (independent variables), factor levels used in 3^2factorial experimental design

Factors	Factor level used		
	-1	0	1
X_1=Concentration of Ethyl cellulose(mg)	300	500	700
X_2=Concentration of PVA (% w/v)	0.5	1.0	1.5

Table-2: Formulation code for preparation of various microballoons compositions by 3^2 design

Formulation Code	Independent variable			
	Coded		Uncoded	
	X_1	X_2	X_1	X_2
DP1	-1	-1	300	0.5
DP2	-1	0	300	1
DP3	-1	1	300	1.5
DP4	0	-1	500	0.5
DP5	0	0	500	1
DP6	0	1	500	1.5
DP7	1	-1	700	0.5
DP8	1	0	700	1
DP9	1	1	700	1.5

Percentage Practical Yield, Percentage Entrapment Efficiency (% EE), Percentage Drug Loading Efficiency and Percentage Buoyancy after 6 hr.

Percentage Practical Yield, Percentage Entrapment Efficiency (% EE), Percentage Drug Loading Efficiency and Percentage buoyancy after 6 hr are shown in the Table-3 and represented graphically in Figure 5, 6, 7 and 8.

Table-3: % Practical yield, % Entrapment Efficiency, %Drug Loading Efficiency and %Buoyancy after 6hr of Telmisartan Microballoons

Formulation	%Practical yield	%E.E	% Drug Loading Efficiency	%Buoyancy after 6 hr
DP1	80.00 ± 0.90	93.60 ± 0.60	29.15 ± 0.40	72.91 ± 0.5
DP2	82.50 ± 0.50	80.20 ± 0.70	24.43 ± 0.41	70.83 ± 0.7
DP3	80.00 ± 1.00	59.41 ± 1.00	18.40 ± 0.15	68.75 ± 0.5
DP4	91.66 ± 0.66	95.09 ± 0.50	15.59 ± 0.34	85.10 ± 0.5
DP5	91.66 ± 0.70	93.57 ± 1.02	15.55 ± 0.28	81.25 ± 0.8
DP6	93.33 ± 0.60	68.98 ± 0.90	12.50 ± 0.25	79.16 ± 0.6
DP7	91.25 ± 0.25	94.21 ± 0.55	12.50 ± 0.40	83.67 ± 0.5
DP8	92.50 ± 0.50	83.03 ± 0.95	10.46 ± 0.40	81.25 ± 0.4
DP9	95.00 ± 1.00	75.74 ± 0.80	9.59 ± 0.33	77.55 ± 0.5

n=3

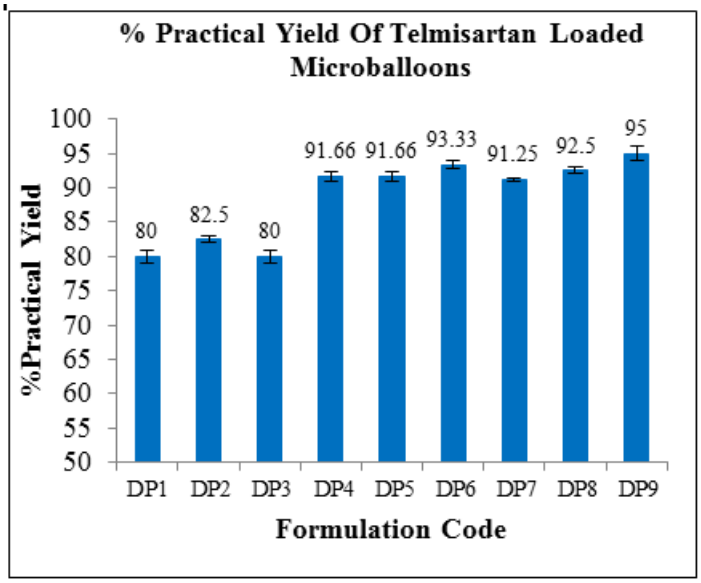

Fig-5: % Practical Yieldof Telmisartan Loaded Microballoons

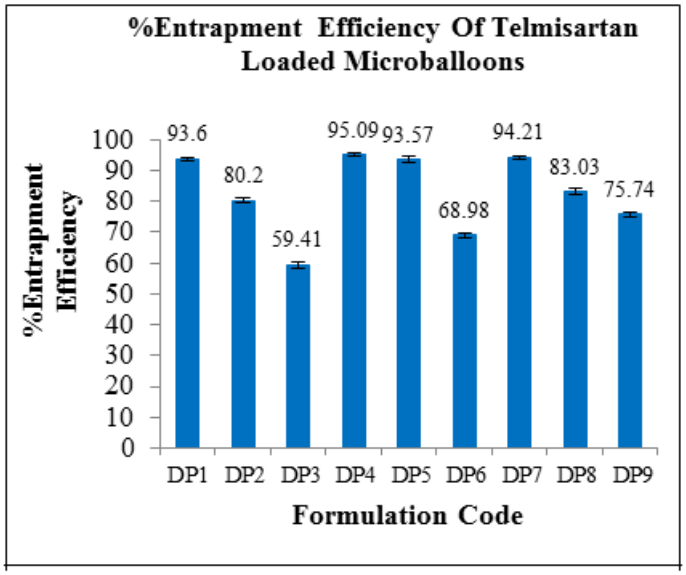

Fig-6: Entrapment Efficiency of Telmisartan Loaded Microballoons

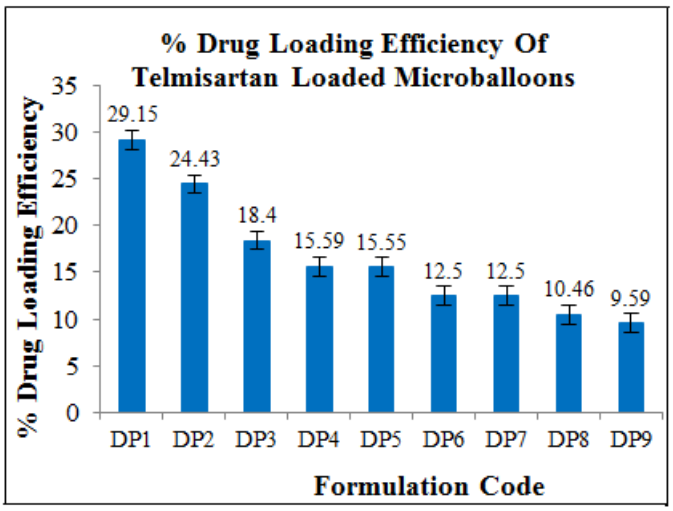

Fig-7: %Drug Loading Efficiency of Telmisartan Loaded Microballoons

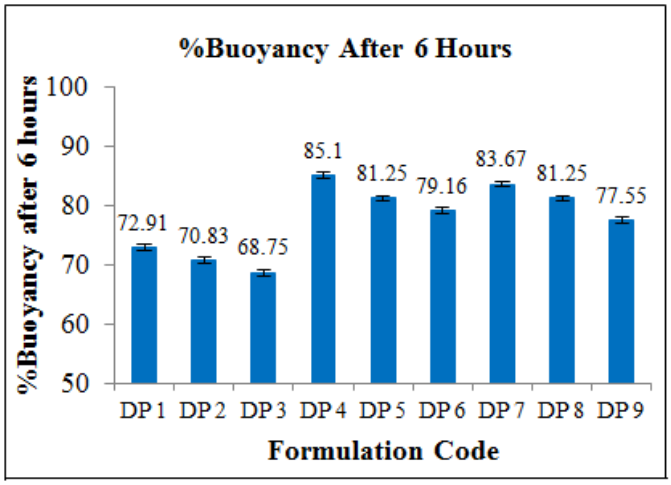

Fig-8: % Buoyancy After 6 hr of Telmisartan Loaded Microballoons

Contour plots and Response surface plots

Contour plots were established between X_1 and X_2 at fixed level of -1, 0 and 1. And they are diagrammatically represented in Figure 9 and 11. By establishment of two dimensional contour plots, the relationship between independent and dependent variables can be explained.

Response surface plots are very helpful in learning about both the main and interaction effects of the independent variables. This is shown in Figure 10 and 12.

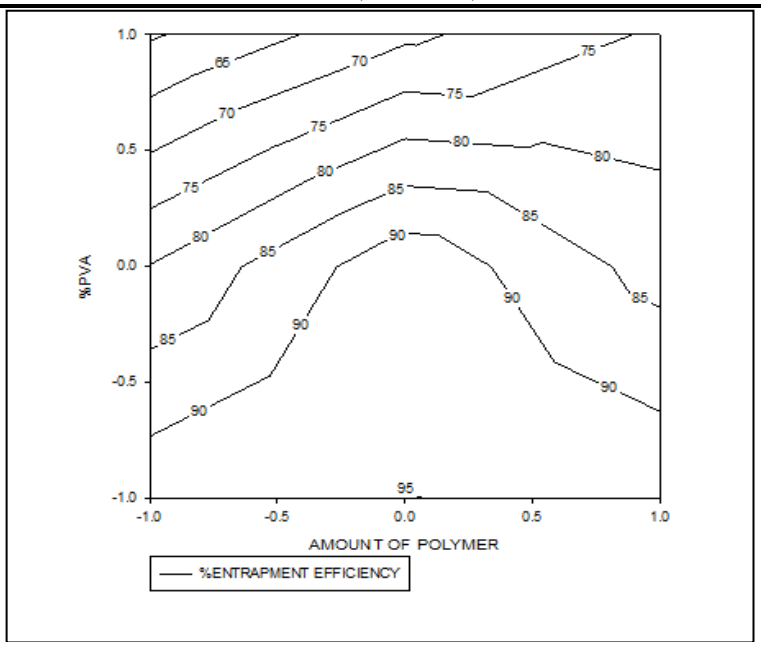

Fig-9: Contour plot showing the effect of amount of Ethyl cellulose (X_1) and concentration of PVA(%w/v) (X_2) on response Y_1 (% Entrapment efficiency)

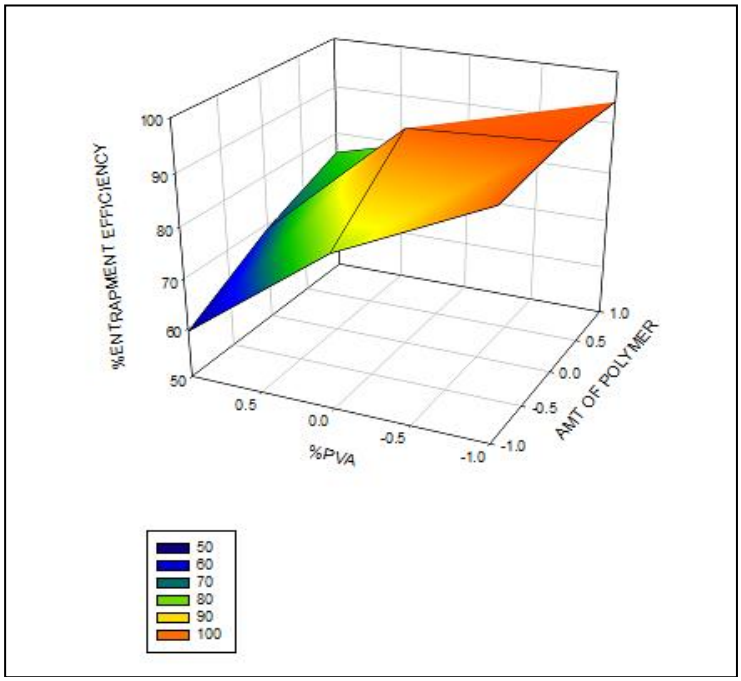

Fig-10: Response surface plot showing the effect of amount of Ethyl cellulose (X_1) and concentration of PVA (%w/v) (X_2) on response Y_1 (% Entrapment efficiency)

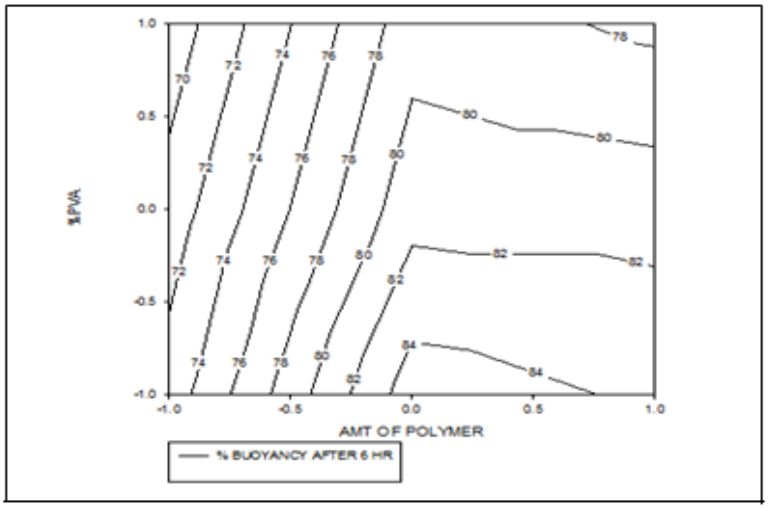

Fig-11: Contour plot showing the effect of amount of Ethyl cellulose (X_1) and concentration of PVA(%w/v) (X_2) on response Y_2 (% Buoyancy after 6 hours)

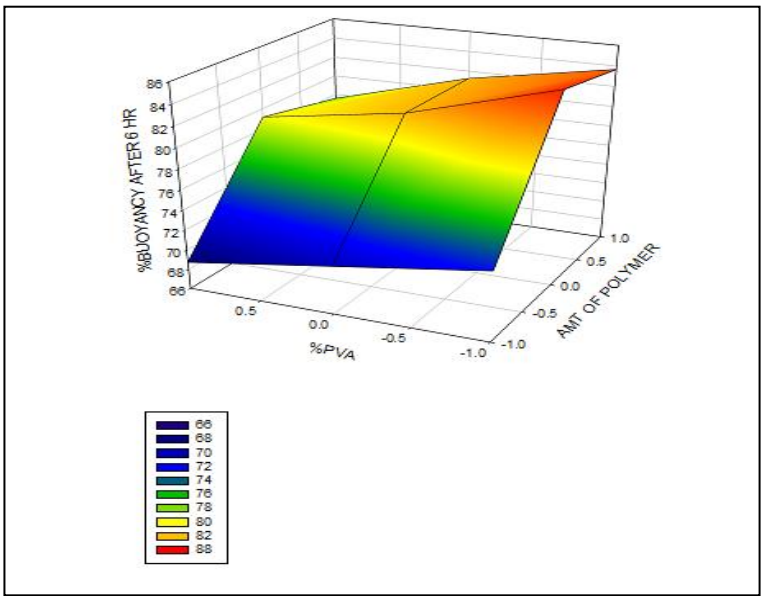

Fig-12: Response surface plot showing the effect of amount of Ethyl cellulose (X_1) and concentration of PVA (%w/v) (X_2) on response Y_2 (% Buoyancy after 6 hours)

Overlay Plot

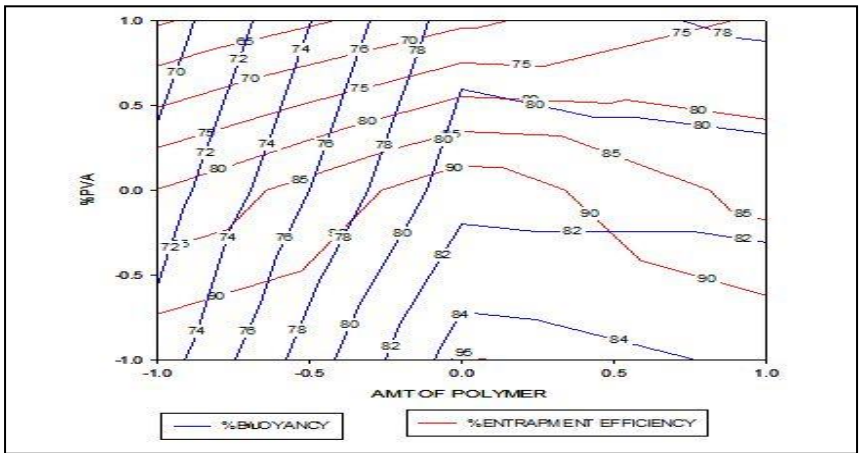

Fig-13: Overlay plot of % Entrapment and % Buoyancy after 6 hr

Buoyancy (%)

Table 4: % Buoyancy after 6 hr

Formulation	1 hr	2 hr	4 hr	6 hr
DP1	91.83 ± 0.6	83.67 ± 0.5	79.16 ± 0.7	72.91 ± 0.5
DP2	89.58 ± 0.4	81.63 ± 0.4	77.08 ± 0.5	70.83 ± 0.7
DP3	85.71 ± 0.7	79.59 ± 0.5	75.00 ± 0.6	68.75 ± 0.5
DP4	95.91 ± 0.5	91.83 ± 0.7	87.50± 0.4	85.10 ± 0.5
DP5	93.87 ± 0.8	89.79 ± 0.5	85.41 ± 0.5	81.25 ± 0.8
DP6	91.83 ± 0.5	89.58 ± 0.3	83.33 ± 0.5	79.16 ± 0.6
DP7	96.00 ± 0.3	93.87 ± 0.4	87.75 ± 0.5	83.67 ± 0.5
DP8	94.00 ± 0.6	91.83 ± 0.8	85.71 ± 0.5	81.25 ± 0.4
DP9	91.66 ± 0.5	85.41 ± 0.5	81.63 ± 0.5	77.55 ± 0.5

n=3

In Vitro Release Study

The in vitro release study carried out for a period of 1 to 12 hrs.

Table-5: % Cumulative Release Data of formulation DP4

Time(hr)	%CDR	Time(hr)	%CDR
1	6.85±0.15	7	61.80±0.40
2	13.29±0.29	8	80.90±0.70
3	19.99±0.20	9	92.35±0.35
4	33.12±0.12	10	93.98±0.70
5	43.59±0.40	11	95.25±0.25
6	56.35±0.35	12	95.73±0.20

n=3

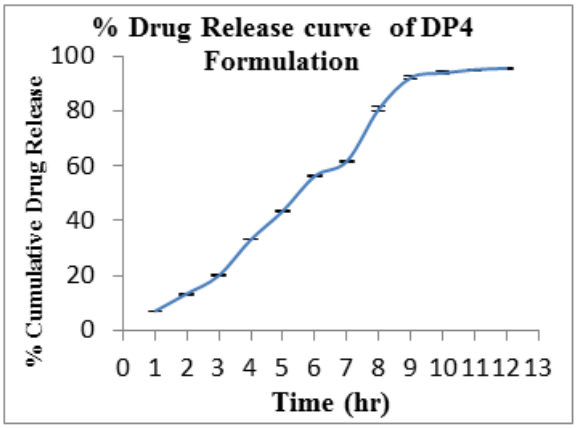

Fig-14: % Drug Release Curve of DP4 Formulation

Process Optimization

Process optimization of Formulation DP4 has been done by 3^2 factorial designs

Selection of Formulation

Formulation was selected on the basis of Formulation Optimization

Table-6: Factors (independent variables), factor levels used in 3^2factorial experimental design

Factors	Factor level used		
	-1	**0**	**1**
X_1= Stirring Speed (RPM)	1300	1500	1700
X_2=Stirring Time (hr)	1	2	3

Table-7: Formulation code for preparation of various microballoons compositions by 3^2 design and summary of response data

Formulation Code	Independent variable			
	Coded		Uncoded	
	X_1	X_2	X_1	X_2
DP10	-1	-1	1300	1
DP11	-1	0	1300	2
DP12	-1	1	1300	3
DP13	0	-1	1500	1
DP14	0	0	1500	2
DP15	0	1	1500	3
DP16	1	-1	1700	1
DP17	1	0	1700	2
DP18	1	1	1700	3

Percentage Practical Yield, Percentage Entrapment Efficiency (% EE), Percentage Drug Loading Efficiency and Percentage Buoyancy after 6 hr.

Percentage Practical Yield, Percentage Entrapment Efficiency (% EE), Percentage Drug Loading Efficiency and Percentage Buoyancy after 6 hr are shown in the Table 8 and represented graphically in Figure 15, 16, 17 and 18.

Table-8: % Practical Yield of Telmisartan Microballoons

Formulation Code	%Practical Yield	%E.E	% Drug Loading Efficiency	% Buoyancy after 6 hr
DP10	83.33 ± 0.65	82.73 ± 0.50	16.65±0.51	89.58 ± 0.6
DP11	78.33 ± 0.33	91.14 ± 0.20	19.32±0.22	85.71 ± 0.5
DP12	80 ± 0.20	94.75 ± 0.75	19.69±0.42	89.36 ± 0.8
DP13	78.33 ± 0.50	94.53 ± 0.40	19.82±0.33	87.75 ± 0.5
DP14	81.66 ± 0.75	95.53 ± 0.50	20.00±0.44	85.41 ± 0.7
DP15	71.66 ± 0.60	96.87 ± 0.30	22.27±0.32	91.83 ± 0.6
DP16	85 ± 0.20	94.80 ± 0.60	18.65±0.44	85.71 ± 0.5
DP17	81.66 ± 0.60	94.97 ± 0.72	19.07±0.32	87.75 ± 0.4
DP18	78.33 ± 0.40	92.51 ± 0.25	19.61±0.18	87.75 ± 0.5

n=3

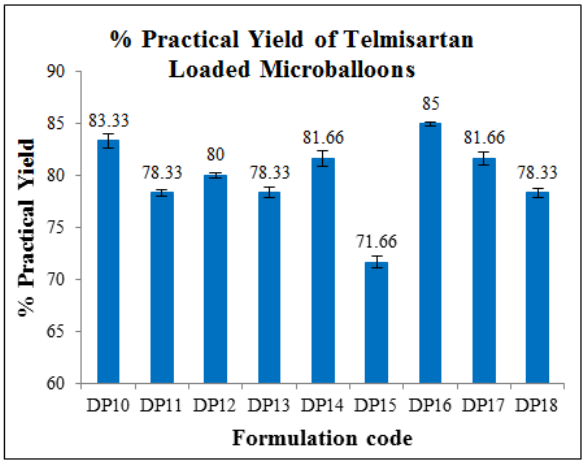

Fig-15: % Practical Yield of Telmisartan Loaded Microballoons

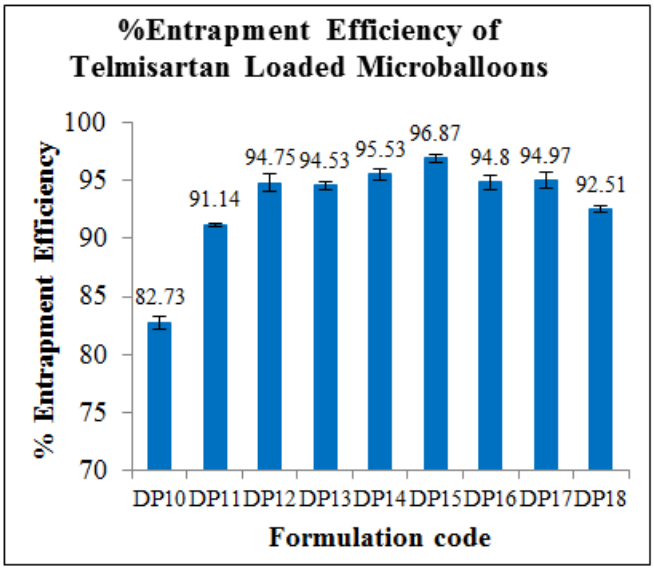

Fig-16: Entrapment efficiency of Telmisartan loaded microballoons

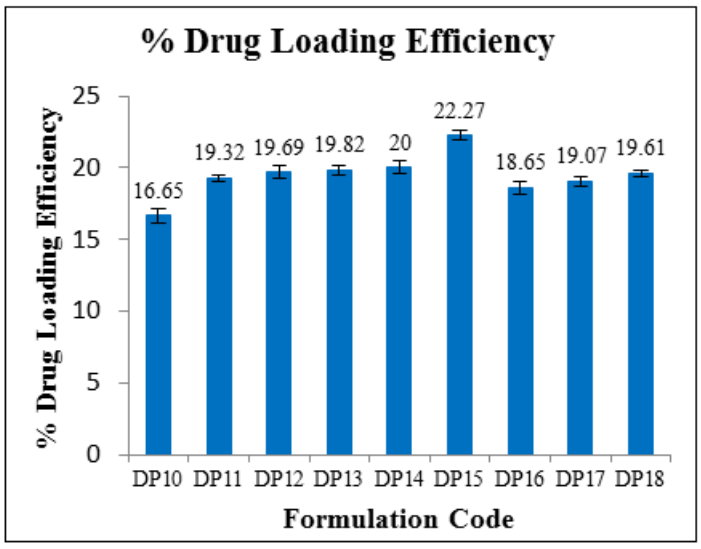

Fig-17: %Drug Loading Efficiency of Telmisartan Loaded Microballoons

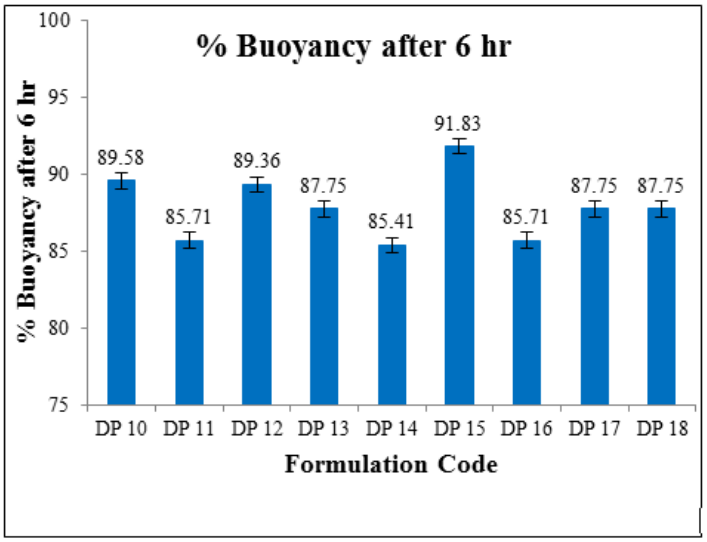

Fig-18: % Buoyancy After 6 hr of Telmisartan Loaded Microballoons

Contour plots and Response surface plots

Contour plots were established between X_1 and X_2 at fixed level of -1, 0 and 1. And they are diagrammatically represented in Figure 19 and 21. By establishment of two dimensional contour plots, the relationship between independent and dependent variables can be explained.

Response surface plots are very helpful in learning about both the main and interaction effects of the independent variables. This is shown in Figure 20 and 22.

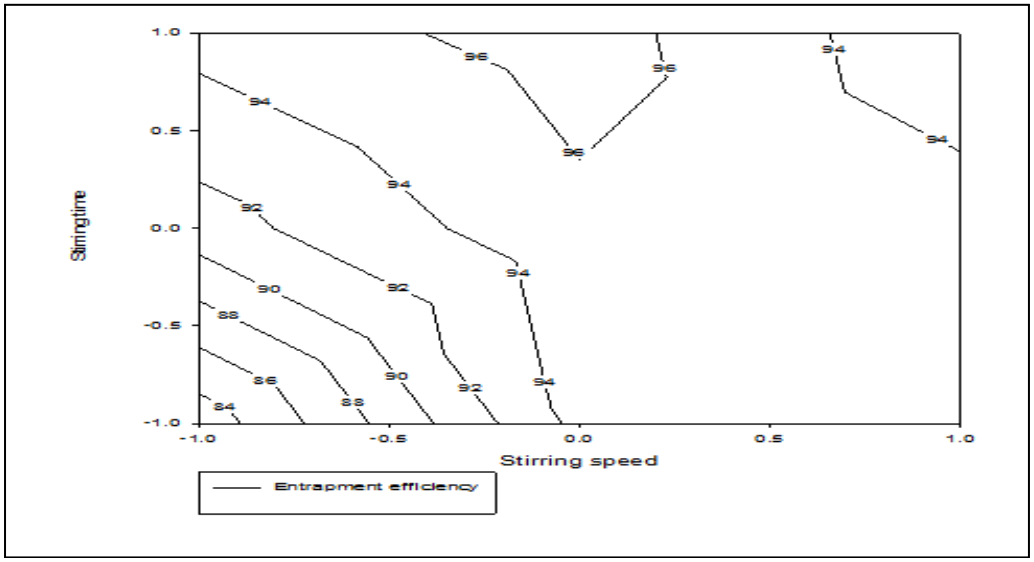

Fig-19: Contour plot showing the effect of stirring speed (X_1) and stirring time (X_2) on response Y_1 (% Entrapment efficiency)

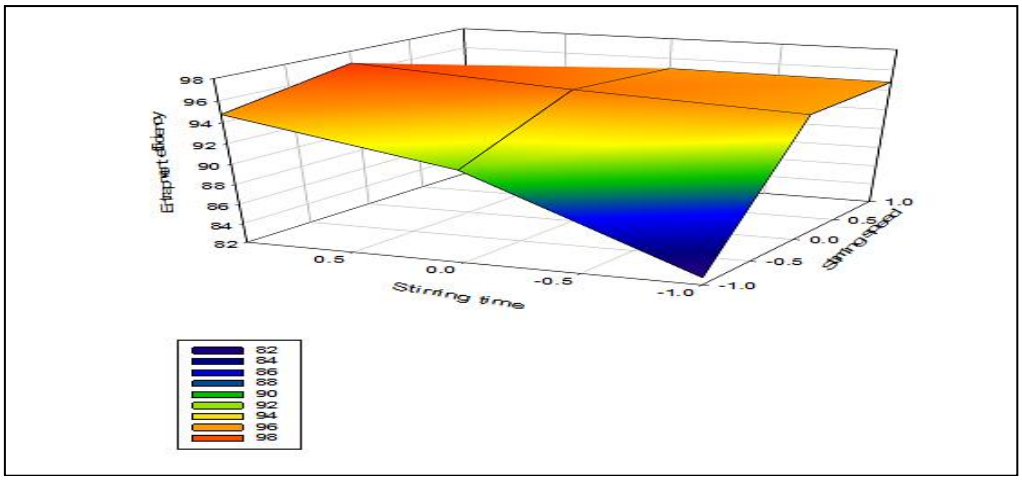

Fig-20: Response surface plot showing the effect of stirring speed (X_1) and stirring time (X_2) on response Y_1 (% Entrapment efficiency)

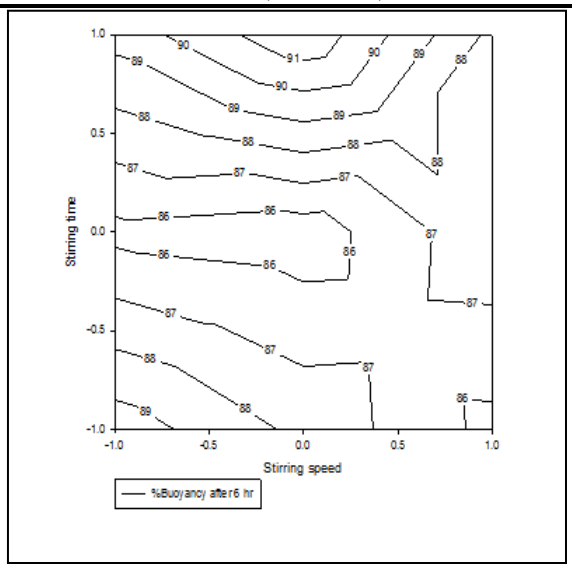

Fig-21: Contour plot showing the effect of stirring speed (X_1) and stirring time (X_2) on response Y_2 (% Buoyancy after 6 hours)

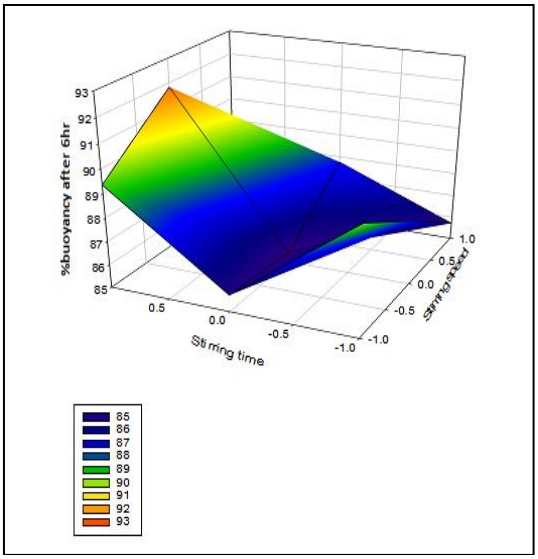

Fig-22: Response surface plot showing the effect of stirring speed (X_1) and stirring time (X_2) on response Y_2 (% Buoyancy after 6 hours)

Overlay Plot

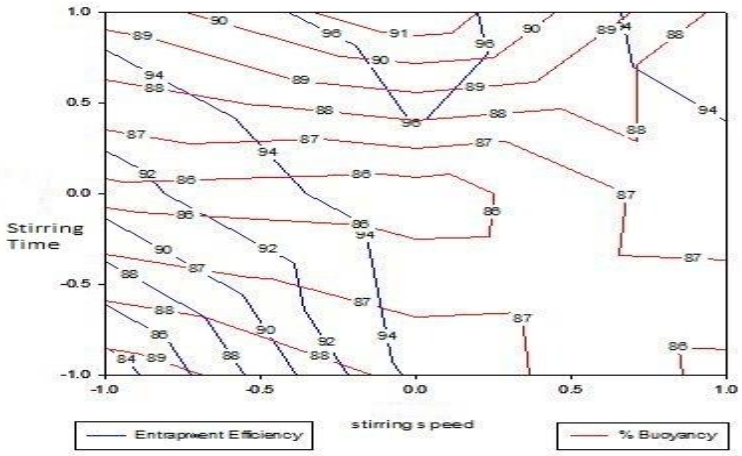

Fig-23: Overlay plot of %Entrapment efficiency and %Buoyancy after 6 hr

Buoyancy (%)

Table-9: % Buoyancy after 6 hr

Formulation	1 hr	2 hr	4 hr	6 hr
DP10	97.95 ± 0.5	93.87 ± 0.4	91.83 ± 0.5	89.58 ± 0.6
DP11	95.91 ± 0.3	91.83 ± 0.6	89.58 ± 0.3	85.71 ± 0.5
DP12	97.91 ± 0.6	95.83 ± 0.7	93.61 ± 0.4	89.36 ± 0.8
DP13	97.95 ± 0.2	95.91 ± 0.6	91.83 ± 0.8	87.75 ± 0.5
DP14	95.91 ± 0.5	93.87 ± 0.5	91.66 ± 0.9	85.41 ± 0.7
DP15	97.95 ± 0.8	95.91 ± 0.4	93.87 ± 0.5	91.83 ± 0.6
DP16	95.91 ± 0.4	91.83 ± 0.7	89.79 ± 0.7	85.71 ± 0.5
DP17	97.97 ± 0.5	93.87 ± 0.4	91.83 ± 0.8	87.75 ± 0.4
DP18	97.95 ± 0.6	93.87 ± 0.3	91.83 ± 0.5	87.75 ± 0.5

n=3

In Vitro Release Study

The in vitro release study carried out for a period of 1 to 12 hrs

Table-10: In vitro diffusion profile of DP13

Time(hr)	%CDR	Time(hr)	%CDR
1	5.34 ±0.3	7	68.08 ± 0.58
2	8.84 ± 0.5	8	85.19 ± 0.19
3	11.68 ± 0.2	9	90.62 ± 0.42
4	16.74 ± 0.24	10	95.00 ± 0.50
5	34.43 ± 0.43	11	97.16 ± 0.16
6	44.04 ± 0.24	12	95.32 ± 0.32

n=3

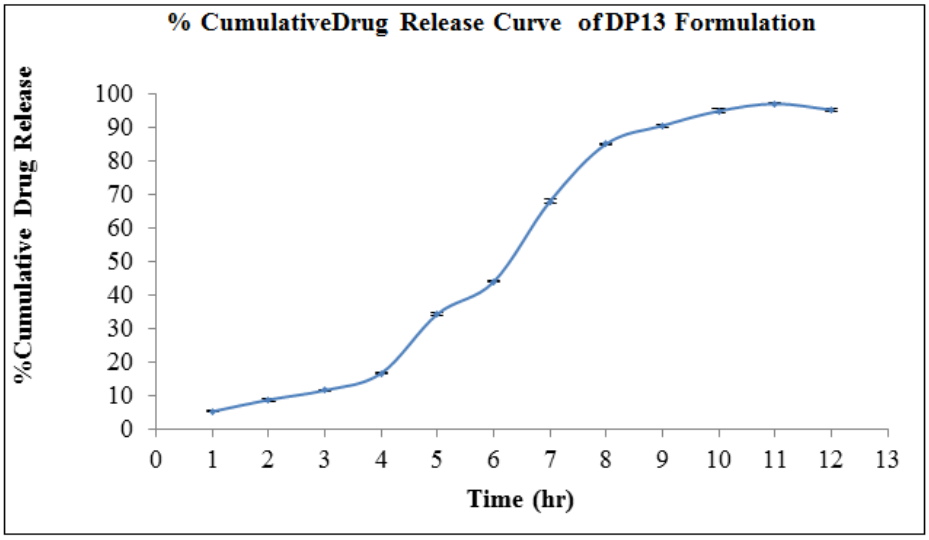

Fig-24: % Cumulative Drug Release Curve of DP13 Formulation

Release Kinetics of Final Optimized Formulation

Various values of the square of regression coefficient for various kinetic models are given in Table-11 and represented graphically in Figure 25, 26, 27 & 28.

Table-11: Release Kinetics of optimized formulation of Telmisartan Loaded microballoons

Optimized formulation	**Higuchi (R^2)**	Zero order (R^2)	First order (R^2)	Korsmeyer peppas (R^2)
DP13	**0.950**	0.937	0.903	0.949

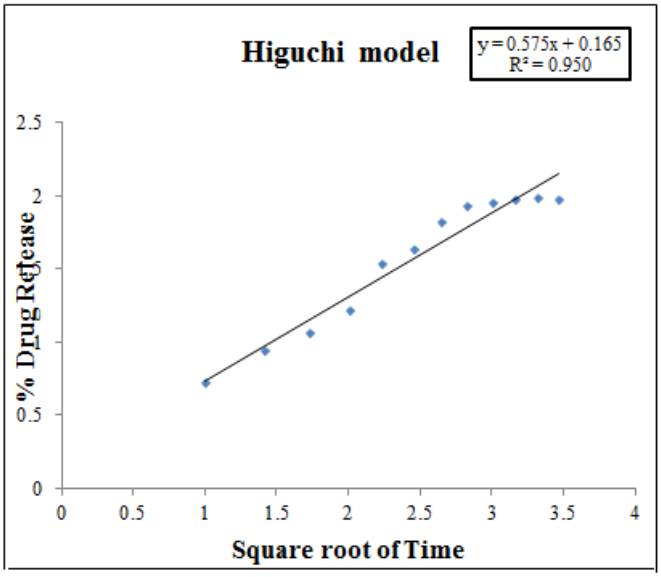

Fig-25: Higuchi model

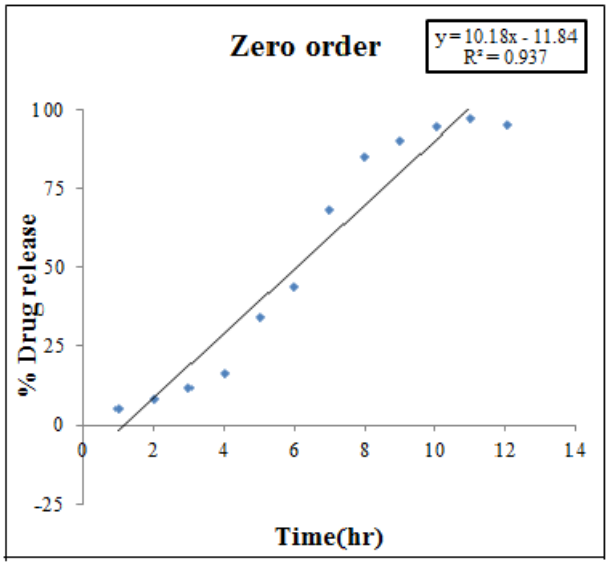

Fig-26: Zero order

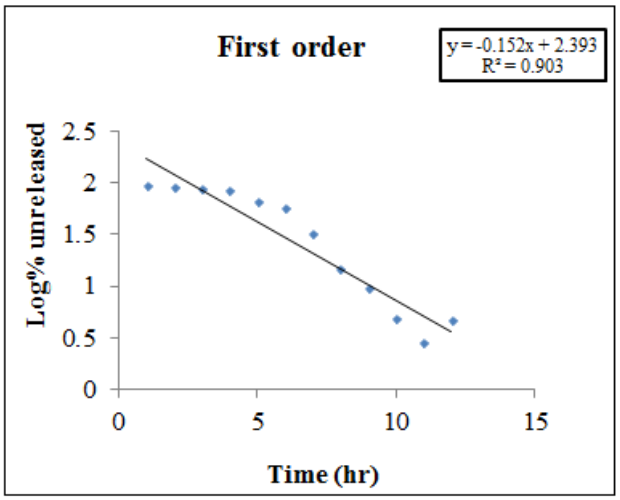

Fig-27: First Order

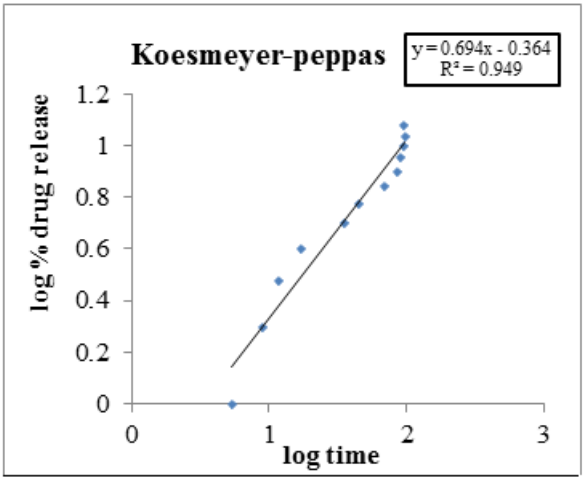

Fig-28: Koesmeyer-Peppas

Morphological Appearance

Fig-29: Flakes Shaped Morphological Appearance of DP15 Formulation (Having Highest Entrapment Efficiency)

Fig-30: Spherical Shaped Morphological Appearance of DP13 Formulation (Optimized Formulation)

Scanning Electron Microscopy

SEM Analysis of Microballoons Loaded Telmisartan.

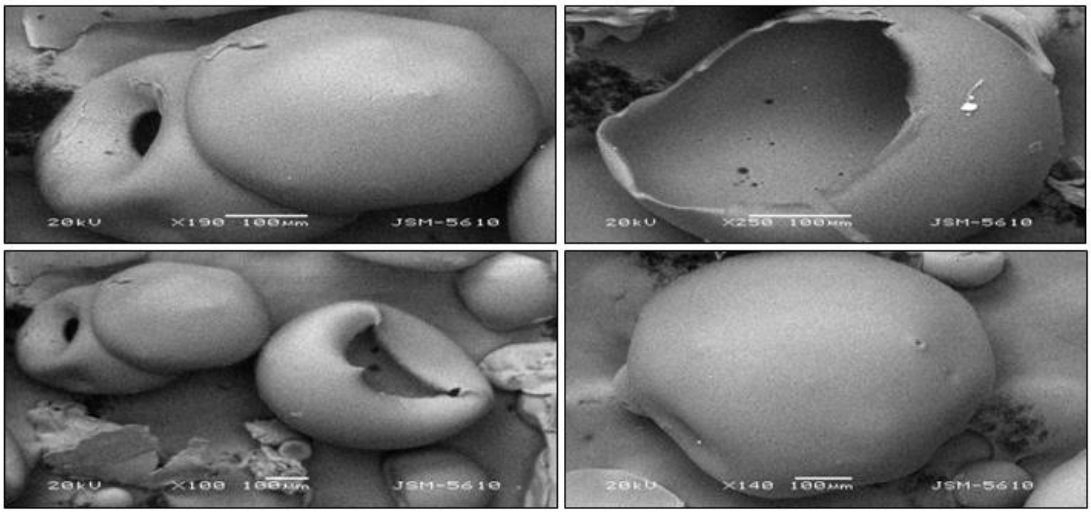

Fig-31: SEM analysis of formulation

Microballoons were hollow and spherical in shape.

X-ray diffraction study

X-ray powder diffraction (XRD) was performed for both pure drug and Optimized formulation of microballons (DP13) to investigate the effect of polymerization on crystallinity of the drug. The disappearance of the characteristic peaks of the drug in the formulation indicated that the drug is dispersed at a molecular level in the polymer matrix.

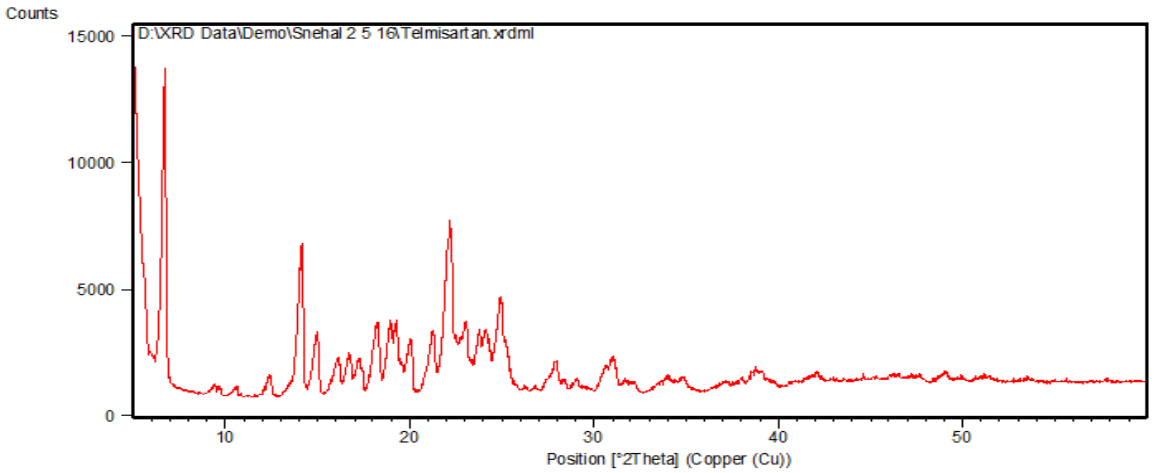

Fig-32: XRD of Telmisartan

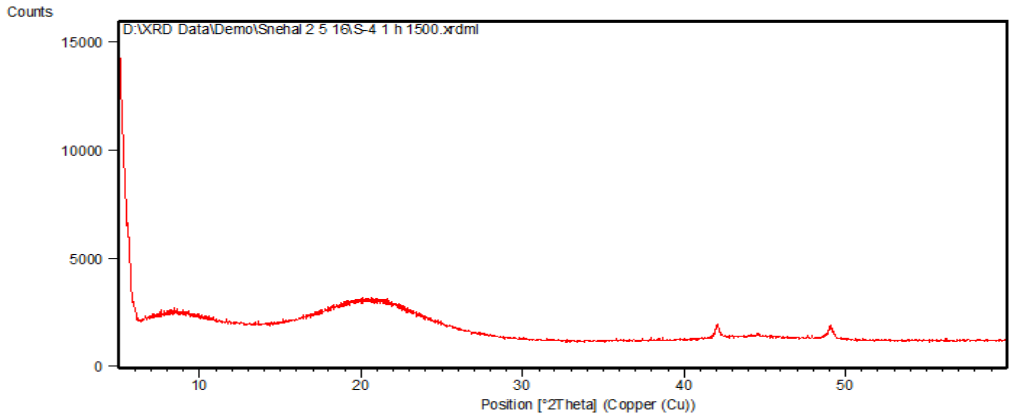

Fig-33: XRD of optimized

Table-12: Compared result of XRD

Sr. No.	Position of 2θ (Drug)	position of 2θ (Microballoons)	Height of peak (Drug)	Height of peak (Microballoons)	% height decrease
1	53.69	54.84	2379.73	348.41	85.35
2	66.85	65.38	4753.01	663.28	86.04
3	100.00	100.00	336.36	19.66	94.15
4	2.86	2.96	680.77	512.83	24.66

Zeta Potential and Particle Size Distribution

Optimized Formulation DP13 was evaluated for Zeta Potential and Particle Size Distribution which was obtained as -41.8mV and 1.344 µm respectively.

Stability study

On the basis of this study it was considered that there was no significant change in the formulation and so we can conclude that formulation was stable after 1 month study at accelerated stability study.

Table-13: Stability Study

Sr. No.	Parameter	Before storage	After 1 month storage (40 ± 2°C / 75% ± 5% RH)	After 1 month storage (30± 2°C / 60% ± 5% RH)	After 1 month storage (2°C -4°C Refrigeration condition)
1	Morphological Appearance	White	White	White	White
2	% Buoyancy (after 6 hours)	87.75	85.20	86.52	87.70
3	% Drug release (12 hours)	95.32	93.96	94.05	94.96

Evaluation of Final Optimized Formulation DP13

Table-14: Evaluation of Final Optimized Formulation DP13

Parameters	Results
% Practical yield	78.33
Particle size	1.344 µm
PdI	1.00
Zeta Potential	-41.8 mV
% Drug Loading Efficiency	19.82
Floating time	>24 hr
% Entrapment	94.53
% Buoyancy	87.75
% drug release at 12 hours	95.32

CONCLUSION

The present research work concludes that the solubility of BCS class II drugs can be enhanced if delivered in the form of microballoons. The microballoons, also facilitates better absorption of the drug from the upper GIT by remaining buoyant. In this work Telmisartan was selected to treat hypertension effectively by formulating microballoons. This drug belongs to BCS class II in which solubility of the drug is a limiting factor for better absorption. An effort was made to formulate microballoons of Telmisartan for improving the solubility and for gastroretention. In this work emulsion solvent diffusion technique was used to develop microballoons of Telmisartan. The research work further concludes that the concentration of polymer ethyl cellulose 500 mg and stabilizer PVA 0.5% w/v play a key role in the optimization of the formula. The % drug entrapment efficiency and % buoyancy vary with the different concentration of the polymer and the stabilizing agent. The factorial design of the formula optimization depicted that the microballoons of the Telmisartan showed high % entrapment efficiency i.e. 95.09 ± 0.5 and maximum % buoyancy after 6 hr i.e.85.10 ± 0.5. The factorial design of process optimization showed that the microballoons of Telmisartan showed high entrapment at 1500 rpm. However rpm had no role in % buoyancy. The influence of the speed on the % Entrapment may be due to the better

mixing of the drug and the polymer along with the appropriate size reduction. The work further concludes that the microballoons of the Telmisartan can be a better drug delivery system for the treatment of hypertension.

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