International Research Journal of Natural and Applied Sciences
ISSN: (2349-4077)
Impact Factor 7.032 Volume 11, Issue 03, March 2024
Website- www.aarf.asia, Email : editor@aarf.asia , editoraarf@gmail.com
Association of Academic Researchers and Faculties (AARF)

"Formulation and characterization of FDDS of Rosiglitazone maleate"

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ABSTRACT

In the current study, wet granulation with colourful attention and combinations of excipients. We delved everypre-compressional parameter, including angle of repose, bulk viscosity, & Carr's indicator. medicine content, hardness, frangibility, weight change, in vitro dissolving trials, floating rates, and stability examinations were performed on the compressed tablets. FTIR and DSC analyses of medicine and excipient comity showed no substantiation of a chemical or physical commerce. The results showed that Rosiglitazone Maleate floating tablets manufactured with natural goo (Xanthan goo), hydrophilic swellable polymer (HPMC K15M), sodium bicarbonate, tartaric acid, magnesium stearate, talc, and DCP functioned excellently without dicing, circumscribing, or clinging. All phrasings showed satisfactory flotation capability and maintained buoyancy for further than 12 hours, according to in vitro buoyancy trials. According to in vitro trials, the release time increases up to 6, 8, and 10 hours, independently, as the content of HPMC K15M in phrasings F1, F2, and F3 is raised. For phrasings F4, F5, and F6, adding xanthan goo raised the release to 7, 9, and 11 hours, independently. The release was planned to be extended to 8, 10, and 12 hours, respectively, in phrases F7, F8, and F9, with the addition of HPMC K 15 M and Xanthan goo. F9 was discovered to be the finest expression since it could maintain release for over to 12 hours. All phrasings displayed "n" value for Peppa's plot in the range of 0.45 to0.89, demonstrating anomalous transport (non-Fickian prolixity) as the system of medicine release. The bettered expression (F9) was demonstrated to be stable and complete without any contact over the course of 90 days.

KEY WORDS
Rosiglitazone Maleate, Gastro Retentive, Gasrtric Residence Time, Non-Steroidal, Anti-Inflammatory Drugs, Floating

INTRODUCTION

The main goal of oral control DDS design should be to enhance and stabilise bioavailability. The majority of pharmaceutical scientists work on creating the optimal DDS these days. The optimal method should deliver the active medication directly to the targeted place and offer the benefit of a single dosage for the duration of the therapy. Scientists have created a system that works, and this encourages other scientists to create control release systems. Similarly, humans' relatively short gastrointestinal tract (GIT), which usually passes through the stomach and upper portion of the intestine in two to three hours, might result in inadequate drug release from the medication delivery system, which lowers the effectiveness of the treatment that is delivered. Therefore, controlling the location of a DDS in a particular area of the GI tract has benefits for a number of significant medications, such as those with stability issues or those with a limited immersion window in the GIT[1].

ADVANTAGE OF FDDS [2]

- The gastro-retentive systems are profitable for medicines absorbed through the abdominal e.g. antacids, Ferrous salts.
- Acidic substances such as aspirin can cause vexation on the abdominal wall whenever come in contact with it. Henceforth HBS expression might be beneficial for the administration of aspirin & other analogous medicines.

DISADVANTAGE OF FDDS[3]

- Floating type system isn't doable for these medicines that have been stability or solubility problem in G.I. Tract.
- These type systems bear a high position of fluid in the abdominal for medicine delivery which float & work efficiently- fleece, water.

APPLICATION [4,5,6]

- **Sustained medicine delivery:** Hydrodynamically balance system can be remains in the abdominal for long ages & henceforth can be release the medicine over an extended period of time. The problem of short stomach hearthstone time is encountered with orally controlled release expression, henceforth, could be overcome with these type systems. These type systems has bulk viscosity of less than 01 as a result they can float on the stomach content.

- **Site specific medicine delivery:** These type systems are mainly advantages for medicines that are precisely absorbed from abdominal or the proximal portion of the small intestine for ex. Riboflavin, Furosemide & Misoprostal.
- **Absorption enhancement system:** Medicines that have weak bioavailability due to site specific absorption from the upper portion of the G.I. Tract are potential entrants to be formulated as FDDS, thus maximize their absorption. A important increase in the bioavailability of floating type dosage forms can be achieved as related with commercially obtainable dosage forms.
- **Constant blood level maintenance**: These types of systems provided easy way to maintain constant blood level for ease of administration & better patient safety.

AIM & OBJECTIVE OF WORK

The goal of the study to formulate and characterize the floating tablets for Rosiglitazone Maleate by wet granulation method with Xanthan gum, HPMC K15M, as polymers, sodium bicarbonate & tartaric acid as gas producing agent and DCP as diluent and finally to performed the stability studies for improved formulation. The tablets prepared by using generally approved excipients which are compatible with Rosiglitazone maleate.

PLAN OF WORK

- To evaluate the pre compression parameters such as compatibility, bulk density, tapped density angle of repose & compressibility index.
- To evaluate the post-compression parameters such as weight variation, thickness, medicine content, dissolution Lag Time and total dissolution time.
- To perform in-vitro dissolution study & release mechanism by using different release kinetic models.
- Selection of a suitable anti diabetic agent and polymers.
- Formulation of Rosiglitazone Maleate FDDS using polymers like HPMC K15M and Xanthan gum.

MATERIALS & METHODS:

Table No. 1: List of used materials

S. No.	Components
1	Rosiglitazone Maleate
2	HPMC K15M
3	Xanthan gum
5	Sodium bicarbonate
6	Tartaric acid
7	Lactose
8	Talc
9	Magnesium stearate

Table 2: List of instruments used

S. No.	**Instrument**
1	Hot Air oven
2	Tablet punching machine
3	Friability testing apparatus
4	Dissolution test apparatus
5	UV–Visible0spectrophotometer
6	FTIR0
7	Melting point
8	Pfizer hardness tester
9	Stability chamber

EXPERIMENTAL WORK[7,8]

PREFORMULATION STUDIES:

The important pre-requisite in development of any DDS. Pre-formulation study performed on the medicine, which included solubility, determination of melting point, & compatibility studies.

Melting point determination:

Melting point of Rosiglitazone Maleate determined by using capillary method.

Solubility:

Solubility of Rosiglitazone maleate determined in water, 0.1M HCL, methanol, acetone.

Compatibility studies by FTIR

Compatibility with polymers confirmed by performing FTIR studies. The Rosiglitazone Maleate & its formulations with polymers subjected to I.R. studies. In the current study, the pellet (potassium bromide disc) method was used.

Compatibility studies by DSC

Individual coils are heated and cooled at the same rate heat DSC in which sample and reference containers are not contiguous and heated them separately. Platinum resistance thermos-meters display the temp. of the sample and reference holders & electronically keep the temp. of the two holders constant. The thermal analysis of medicine and medicines - excipients mixtures, DSC used. Individual samples (medicine and identified excipients (passed via 60 mesh Sieve) & weighed directly in the pierced DSC Alu pan & scanned between temperature range of 50°C to 300°C (along with heating rate of 10°C/minute) under dry nitrogen atmosphere.

Determination of λ_{max}

The solution of Rosiglitazone Maleate contains the conc. 10 µg/ml prepared in 0.1 M HCL & UV-VIS spectrum was taken using Shimadzu (UV-1601) double beam spectro-photometer. The solution scanned in range between 200 – 400 nm.

Preparation for standard calibration curve of Rosiglitazone Maleate

Stock I: 100mg of Rosiglitazone Maleate was precisely weighted into 100ml volumetric flask & dissolved in 0.1M HCL after that volume made up with 0.1M HCL.

Stock II: Take Pipette of 1ml of aforementioned solution into another 10ml volumetric flask & the volume made up with 0.1M HCL. Aliquot part of, 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, 2.5 ml, 3.0 ml from standard drug solution were diluted into 10 ml with 0.1M HCl. The absorbance of mentioned solutions measured at 318nm taken 0.1M HCL as a blank.

DOSE CALCULATION[9]

For SR drug up to 12 hours, the total dose of medicine required was calculated basis on the fact that the conventional dose calculated using the below mentioned equation:

$D_t = Dose0(1+0.693 \times t/t_{½})$

D_t = Total0dose, Dose= Immediate0release dose, t=0Total time0period for which SR is required, $t_{½}$ = shelf-life of medicine. For Rosiglitazone Maleate: D_t=0Dose (1+0.693 × 12/3.5), D_{t0}=6.752mg Rosiglitazone & 8.9430 mg of Rosiglitazone Maleate is equivalent to 6.7520 mg Rosiglitazone.

METHOD OF PREPARATION[10]

The composition of different-different formulations of Rosiglitazone Maleate floating tablets is given in Table no. 3. The contents weighed accurately & mixed thoroughly. Granulation activity performed with a binder solution of PVP K-30 in adequate qty. of IPA. The 40 mesh sieved granules were dried in hot air oven at 45.0°C. Drying of the granules completed when the sample reached a loss on drying (LOD) value of 1.0 to 3.0%, as measured by a IR moisture balance at 105°C. Those dried granules passed through suitable sieve i.e. 40/60 mesh, then lubricated with purified talc (1.0 % w/w) and magnesium stearate (2.0% w/w) finally compressed.

Table no. 3: Composition of different formulations

Ingredients in (mg)	0**F1**	0**F2**	0**F3**	0**F4**	0**F5**	0**F6**	0**F7**	0**F8**	0**F9**
RosiglitazoneeMaleate	90	90	90	90	90	90	90	90	90
HPMCeK 15 M	450	540	630	-	-	-	300	22.50	150
Xanthan gum	-	-	-	450	540	630	150	22.50	300
Sodiumebicarbonate	200	200	200	200	200	200	200	200	200
Tartariceacid	100	100	100	100	100	100	100	100	100
PVP-K-e30	04.5	04.5	04.5	04.5	04.5	04.5	04.5	04.5	04.5
Dicalciumephosphate	570	480	390	570	480	390	570	480	390
Magnesium eStearate	30	30	30	30	30	30	30	30	30
eTalc	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
Totaleweight in mg	1500	1500	1500	1500	1500	1500	1500	1500	1500

EVALUATION PARAMETERS[12]

Thickness and diameter

The tablet thickness & diameter measured by using Vernier caliper in mm.

Hardness

The hardness of tablets measured by using Pfizer hardness tester in kg/cm^2.

Weight variation

20 tablets accurately weighed individually & together in a weighing balance. The average weight noted & standard deviation calculated. The tablet passes the test. I.P. specification limit for weight variation of tablets weighing up to 120 mg is ±10%, 120 mg - 300 mg is ±7.5% and more than 300 mg is ±5%.

$$\%\ \text{Weight variation} = \frac{\text{Average weight - Individual weight}}{\text{Average weight}} X100$$

Friability (F):

Tablet strength tested by friabilator (Roche). Initial weighed tablets allowed for 100 revolutions in 04 minute & dedusted. The % weight loss calculated by re-weighing the tablets. The %friability was calculated as per below formula

$$\%\ \text{Friability} = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} X100$$

Floating property:

In-vitro floating determined by the floating pause time. The tablets placed in 100mL beaker filled with 0.1M HCL. The time taken for tablet to rise to the surface for floating determined as the BLT and furthermore floating period of all tablets determined by visual observation.

Medicine Content

Stock solution-I: 20 tablets powdered with help of pestle mortar. Weighed precisely the qty. equivalent to 100mg of Rosiglitazone maleate & transferred in to a 100ml volumetric flask filled with few ml of 0.1M HCL & shake for some time then make up the volume with 0.1M HCL.

stock solution-II: Take Pipette of 10 ml and pipette out I stock solution into another 100ml volumetric flask then make up the volume with 0.1M HCl (i.e. 100 µg/ml).

Aliquots: From the aforementioned solution 1ml quantity (as per Beer's range 5-30 µg/ml) withdraw & the volume made up to 10 ml with 0.1 M HCL. The absorbance measured spectro-photometrically at 318 nm using 0.1 M HCL(as blank).

***In vitro* release studies:**

The rates of release for Rosiglitazone Maleate by floating type tablets evaluated by using USP Paddle type dissolution apparatus. The dissolution test performed by using 900ml of 0.1M HCL, at 37±0.5°C at 50 rpm. Approx 10ml sample of the solution withdrawn from the apparatus every hour for continue 12 hrs, & the withdraw samples replaced with fresh dissolution medium. The samples filtered through Whatman filter paper and measured the absorbance of at 318nm. Dissolution profiles of formulations were analysed by plotting medicine release vs. time graph.

RESULTS & DISCUSSION

RESULTS:

PREFORMULATION STUDY FOR ROSIGLITAZONE MALEATE FLOATING TABLETS

Determination of melting point: Melting point of Rosiglitazone Maleate found to be in the range 122 to 123^0C.

Solubility: Rosiglitazone Maleate free soluble in methanol, 0.1M HCL, sparingly soluble in water and acetone.

Estimation of Rosiglitazone Maleate by UV spectroscopy

Determination of λ_{max}

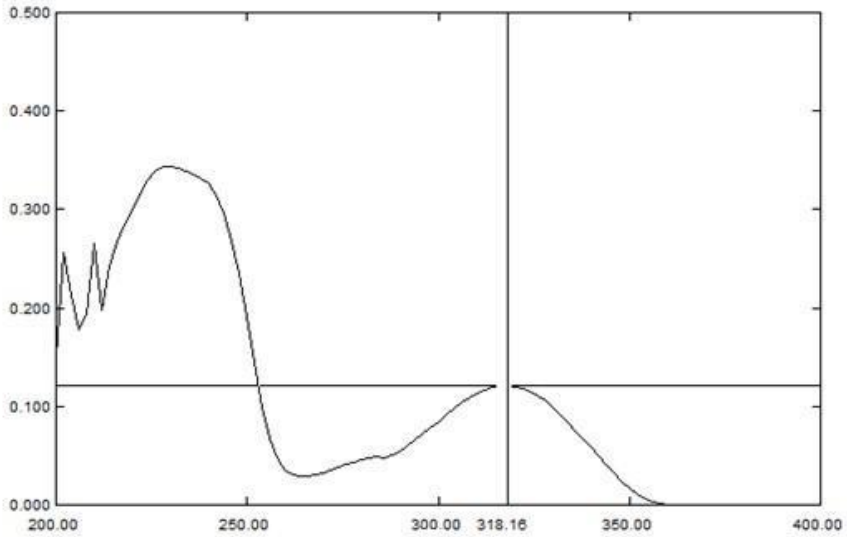

Figure 3: UV spectra of Rosiglitazone Maleate at 10 µg/ml concentration

Table 5: Wavelength of maximum absorption in 0.1M HCL

S. No.	Solvent	max
1	0.1M HCL	318.16

CALIBRATION CURVE

Table 6 : 0**Calibration curve data of Rosiglitazone Maleate in**0**0.1M HCL**

S. Noi	Concentration (µg/ml)	Absorbance at 318 nm
1	00	00
2	50	0.0660
3	100	0.1200
4	150	0.1910
5	200	0.2490
6	250	0.3150
7	300	0.3810

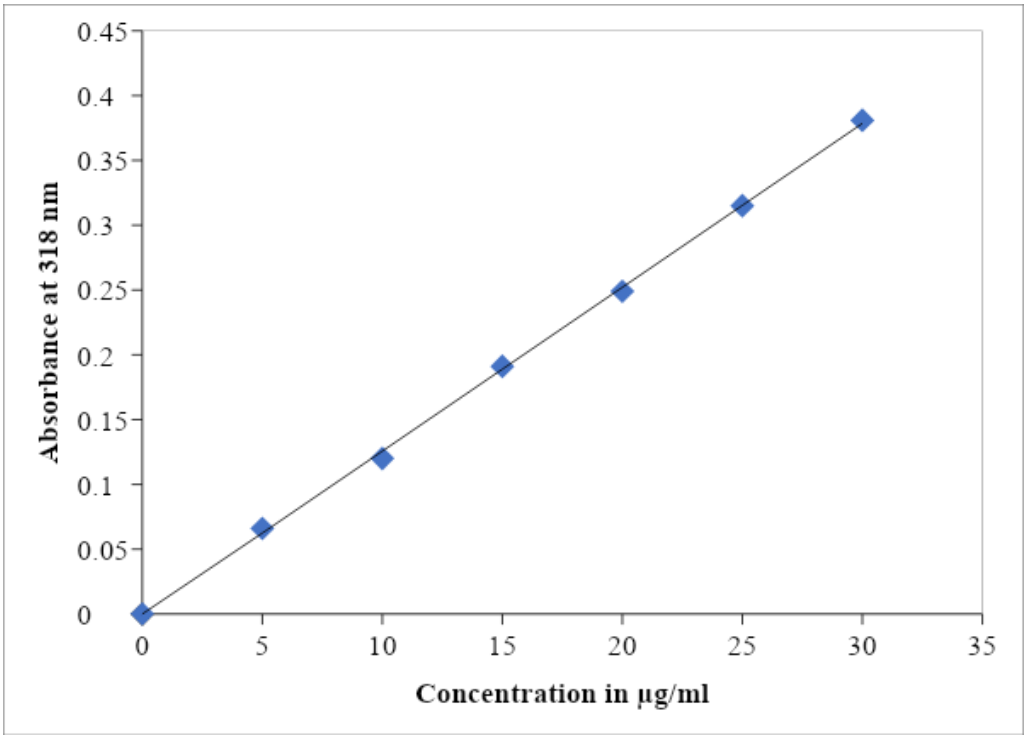

Figure 4: Calibration curve of Rosiglitazone Maleate at 318 nm

Compatibility studies

FTIRispectroscopy

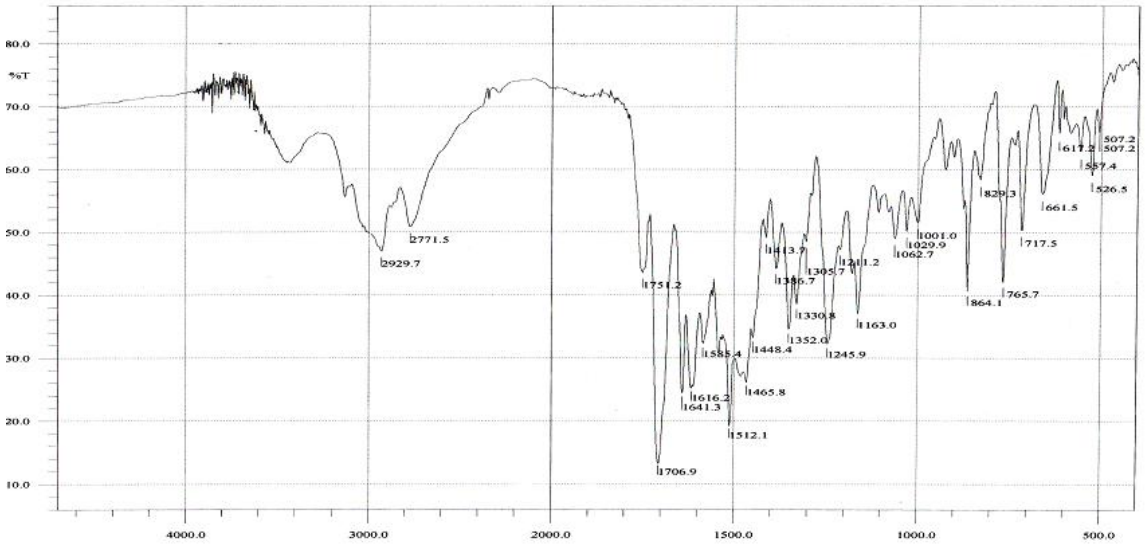

Figure 5: FTIRi spectra of Rosiglitazone Maleate

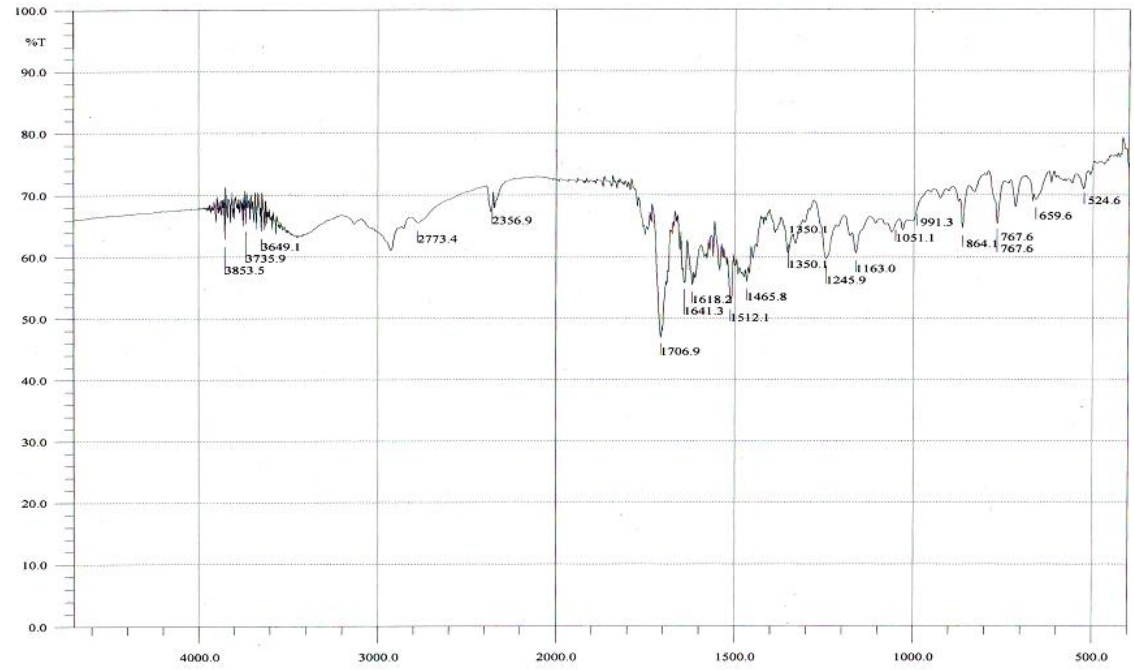

Figure 6: FTIR spectra of ROSIGLITAZONE MALEATE + HPMCi K15M

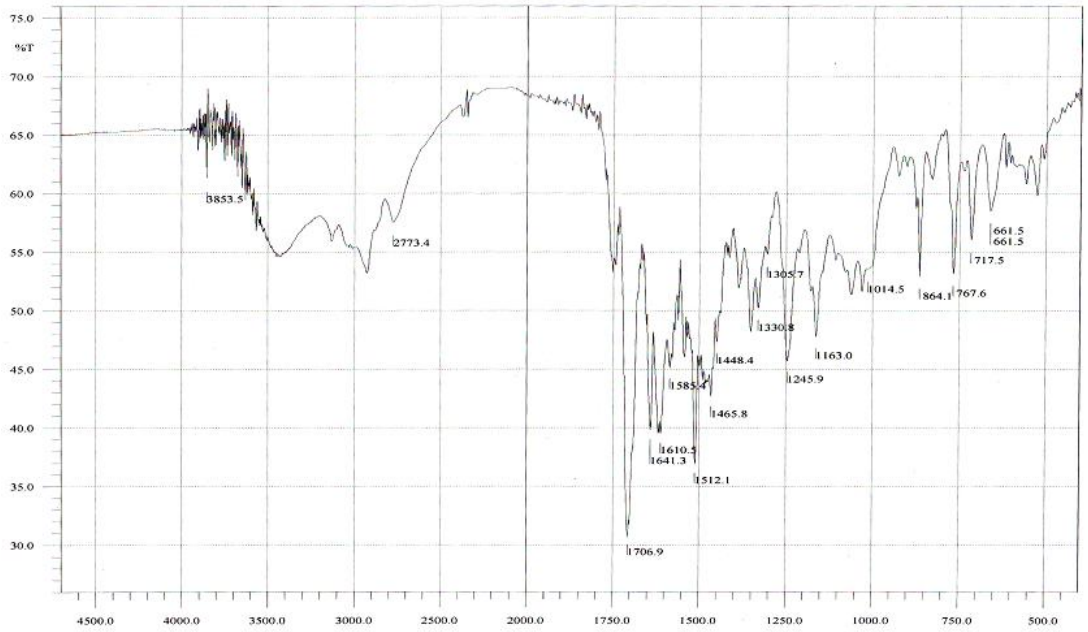

Figure 7: FTIR specra of Rosiglitazone Maleate + Xanthan gum

Evaluation of Rosiglitazone Maleate i **floating tablets**

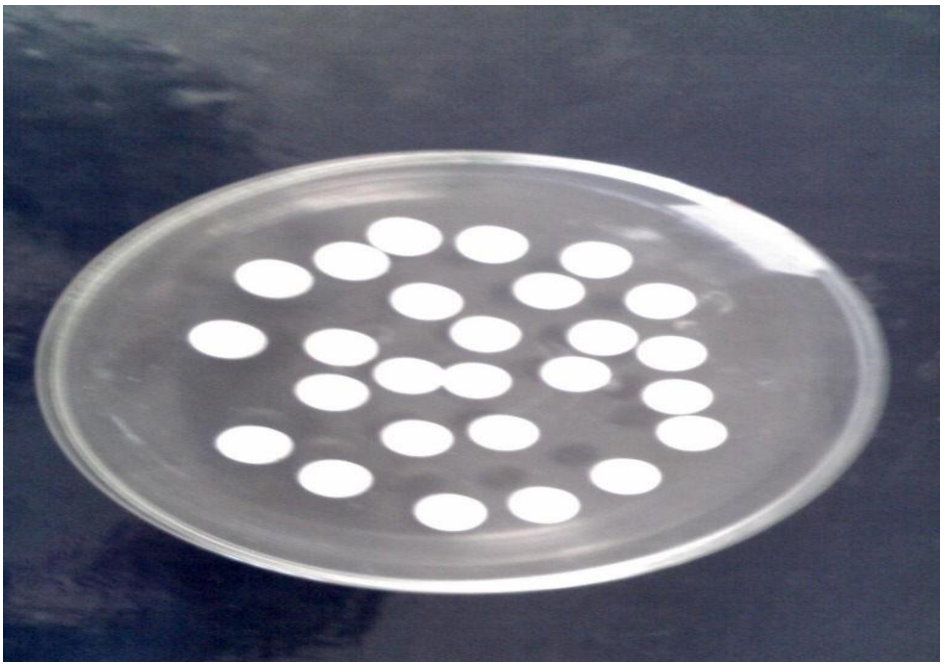

Figure 8: Picture of floating tablet of Rosiglitazone maleate

Table 7: Interpretation of FTIR spectrums of 1) Rosiglitazone Maleate, 2) Rosiglitazone Maleate and HPMC K15M, 3) Rosiglitazone Maleate and Xanthan gum

0**S.No.**	**IR**0**spectrum**	**Groups**	0**Peaks(cm^{-1})**	**Stretching**0 **/Deformation**
1	Rosiglitazone maleate	C=N0	1641.3	Stretchingi
		C-O0	1062.7	Stretchingi
		C=O0	1751.3	Stretchingi
		C=C0	1616.2	Stretchingi
		C-N0	1245.9	Stretchingi
		NH0	3430.51	Stretchingi
		C-H0 (Aromatic)	3053.42	Stretchingi
		C-H0 (alkane)	2929.37	Stretchingi
2.	Physical mixture of Rosiglitazone maleate and HPMC K 15 M	C=N0	1641.3	Stretchingi
		C-O0	1051.7	Stretchingi
		C=O0	1751.3	Stretchingi
		C=C0	1618.2	Stretchingi
		C-N0	1245.9	Stretchingi
		NH0	3430.5	Stretchingi
		C-H0 (Aromatic)	3053.42	Stretchingi
		C-H0 (alkane)	2929.7	Stretchingi
3.	Physical mixture of Rosiglitazone maleate and Xanthan gum	C=N0	1641.3	Stretchingi
		C-O0	1051.3	Stretchingi
		C=O0	1750.0	Stretchingi
		C=C0	1610.5	Stretchingi
		C-N0	1245.9	Stretchingi
		NH	3430.5	Stretchingi
		C-H0 (Aromatic)	3053.42	Stretchingi
		C-H (alkane)	2929.37	Stretching

DSC

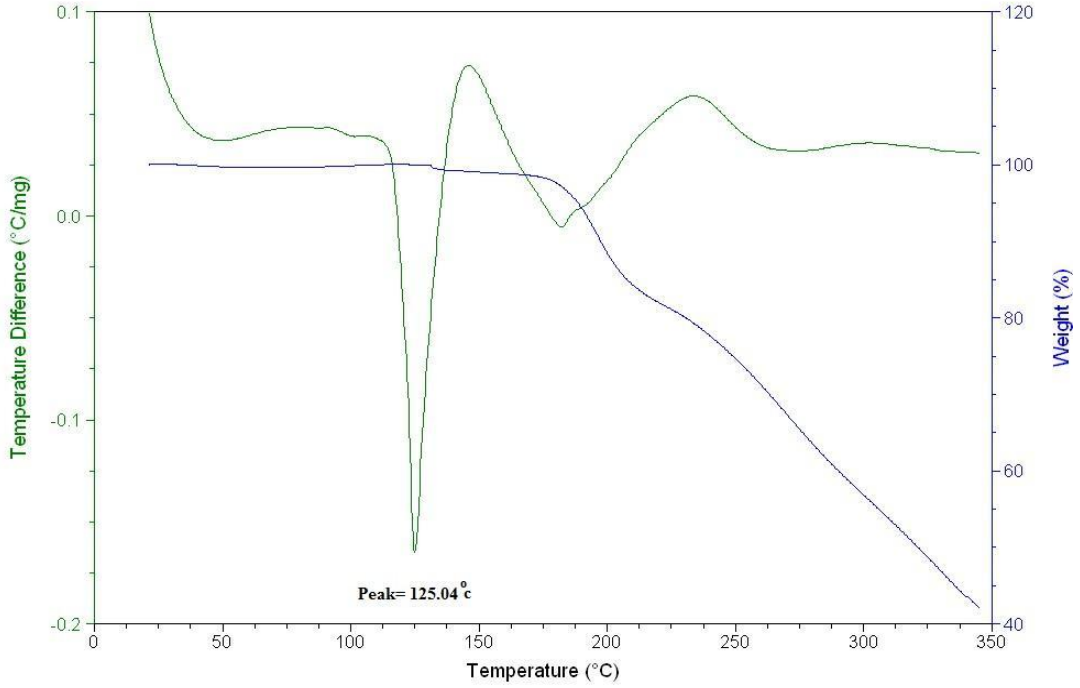

Figure 9: DSC of Rosiglitazone Maleate

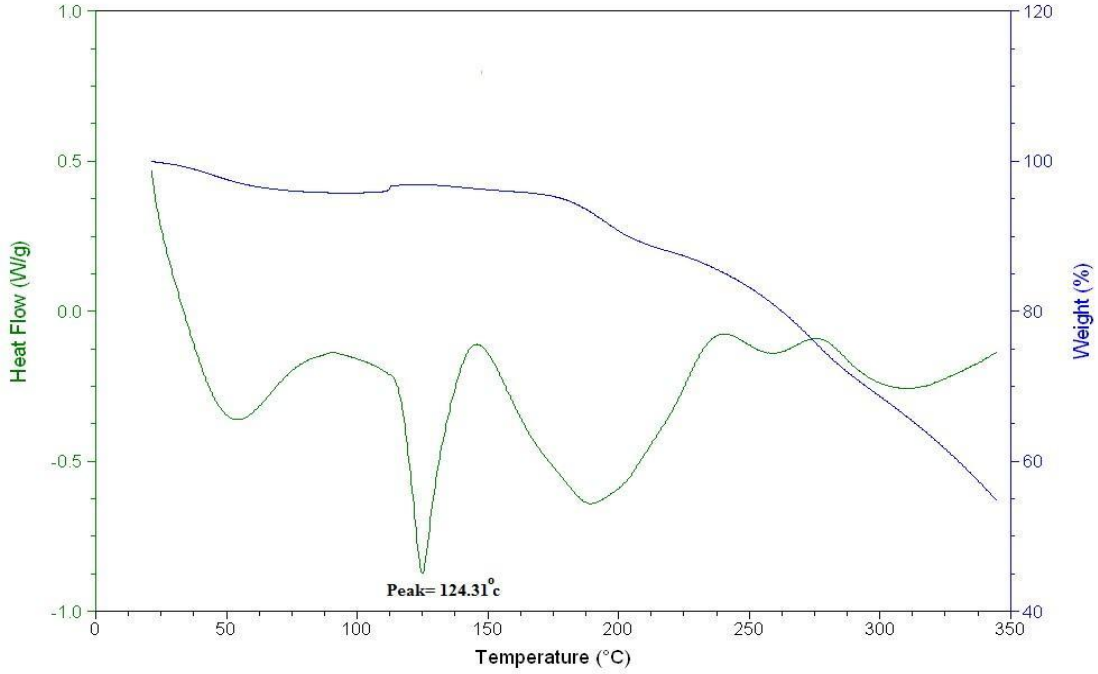

Figure 10: DSC of Rosiglitazone Maleate + HPMC K15 M + Xanthan gum

Pre-compression0evaluation of Rosiglitazone maleate floating0tablets

Table 8: Evaluation of micromeritics properties of the granules

Formulation no.		**Evaluation0parameters**		
	Bulk0density (g/cc) ±0SD	**Tapped0density (g/cc) ±0SD**	**Angle of0repose ±0SD**	**Carr's0index ±0SD**
0F1	0.486 ± 0.0110	0.564 ± 0.0410	$020.1^0 \pm 0.7$	13.82 ± 0.740
0F2	0.483 ± 0.0050	0.578 ± 0.0960	$021.7^0 \pm 1.0$	15.91 ± 0.520
0F3	0.468 ± 0.1130	0.568 ± 0.0130	$023.7^0 \pm 0.4$	17.60 ± 0.790
0F4	0.442 ± 0.0350	0.521 ± 0.0380	$021.5^0 \pm 0.8$	15.16 ± 0.320
0F5	0.443 ± 0.1470	0.531 ± 0.0520	$022.3^0 \pm 0.3$	16.57 ± 0.270
0F6	0.453 ± 0.0120	0.547 ± 0.0160	$023.2^0 \pm 1.2$	17.18 ± 0.130
0F7	0.478 ± 0.0340	0.567 ± 0.0130	$021.7^0 \pm 1.1$	15.69 ± 0.320
0F8	0.473 ± 0.0920	0.569 ± 0.9120	$023.8^0 \pm 0.9$	16.87 ± 0.560
0F9	0.457 ± 0.0010	0.556 ± 0.8210	$023.9^0 \pm 0.4$	17.80 ± 0.830

SD=0Standard deviation (n=3)

Post compression parameters

Table 9: Post-compression evaluation of Rosiglitazone Maleate floating tablets

Formulation code		Evaluation parameters		
	Thickness0 ± SD (mm)	Hardness0 ± SD (kg/cm^2)	Friability0 (%) ± SD	Average weight0variation ± SD
0F1	02.80 ± 0.021	03.9 ± 0.1	0.359 ± 0.050	0.149 ± 0.5770
0F2	02.82 ± 0.034	04.2 ± 0.1	0.678 ± 0.020	0.149 ± 1.5270
0F3	02.80 ± 0.012	04.1 ± 0.1	0.420 ± 0.080	0.148 ± 0.5770
0F4	02.81 ± 0.001	04.2 ± 0.1	0.399 ± 0.030	0.151 ± 0.8210
0F5	02.83 ± 0.005	04.2 ± 0.1	0.566 ± 0.010	0.152 ± 0.6340
0F6	02.80 ± 0.011	04.3 ± 0.1	0.481 ± 0.060	0.149 ± 1.2310
0F7	02.82 ± 0.013	04.2 ± 0.1	0.644 ± 0.090	0.149 ± 0.9120
0F8	02.81 ± 0.016	04.1 ± 0.1	0.455 ± 0.030	0.151 ± 0.5770
0F9	2.80 ± 0.003	4.3 ± 0.1	0.483 ± 0.05	0.149 ± 1.527

SD=0Standarddeviation (n=3)

Medicine content uniformity of Rosiglitazone Maleate floating tablets

Table 10: Medicine content uniformity of Rosiglitazone.Maleate floating tablets

Tablet formulation	Calculated value0(mg)	Estimated value0 (mg)±SD	%0Drug content ±SD
0F1	09	08.677 ± 0.003	095.78 ± 0.007
0F2	09	08.591 ± 0.006	095.45 ± 0.002
0F3	09	08.602 ± 0.006	095.7 ± 0.005
0F4	09	08.422 ± 0.005	095.76 ± 0.006
0F5	09	08.603 ± 0.005	095.57 ± 0.004
0F6	09	08.702 ± 0.005	096.63 ± 0.001
0F7	09	08.678 ± 0.004	096.47 ± 0.006
0F8	09	08.744 ± 0.006	097.16 ±0.008
0F9	09	08.812 ± 0.009	097.91 ± 0.05

SD=Standard deviation (n=3)

Floating property of Rosiglitazone Maleate floating tablets

Table 11: Results of floating property of Rosiglitazone Maleate tablets

Formulation no.	**Floating lag0time (S)**	0**Total floating0time (h)**
0F1	025.33 ±1.52	>120
0F2	047.0 ± 1.0	>120
0F3	068.6 6 ± 0.57	>120
0F4	072.66 ± 2.08	>120
0F5	0115.0 ± 2.0	>120
0F6	0147.66 ± 2.08	>120
0F7	031.33 ± 1.52	>120
0F8	053.0 ± 2.0	>120
0F9	74.0 ± 1.0	>120

SD= Standard8deviation(n=3)

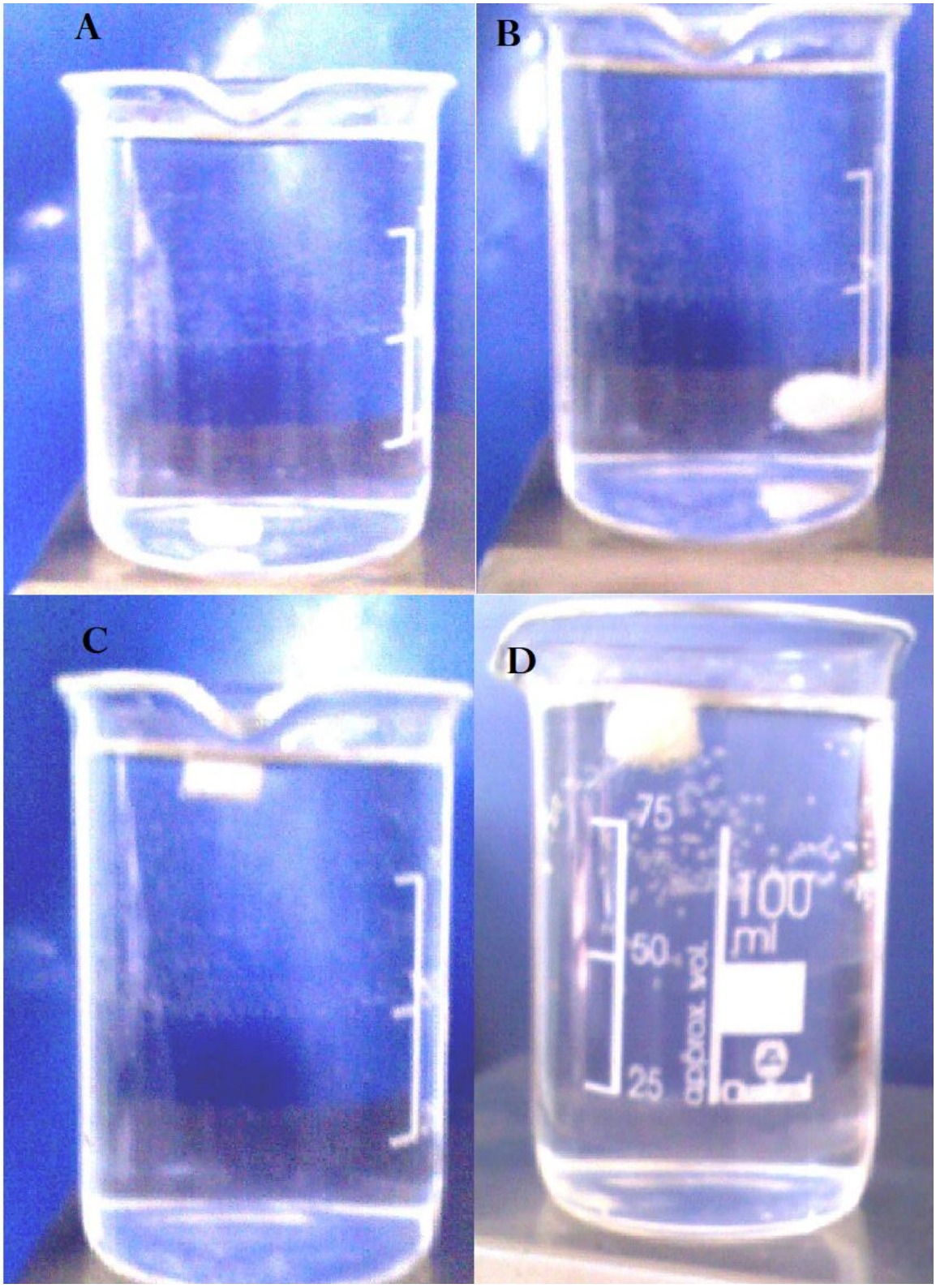

Figure 11:Floating lagtime (F9) A) Initial B) At 25 Sec C) 74 Sec D) At 12 hours

Table 12: Invitro medicine release data of F1 to F4 formulations

Time in hr	% Cumulative medicine release			
	F1±SD	**F2±SD**	**F3±SD**	**F4±SD**
0	0	0	0	0
1	42.5 ± 0.40	34.58 ± 0.47	29.52 ± 0.41	37.78 ± 0.32
2	63.16 ± 0.23	46.77 ± 0.32	42.34 ± 0.51	57.54 ± 0.42
3	78.25 ± 0.29	57.58 ± 0.37	57.46 ± 0.40	69.48 ± 0.33
4	87.69 ± 0.50	68.38 ± 0.46	69.22 ± 0.17	78.43 ± 0.49
5	93.43 ± 0.31	79.65 ± 0.34	76.32 ± 0.49	86.40 ± 0.27
6	98.14 ± 0.18	88.56 ± 0.40	82.52 ± 0.39	92.44 ± 0.38
7	-	93.44 ± 0.29	87.5 ± 0.42	98.34 ± 0.32
8	-	98.55 ± 0.40	91.62 ± 0.3	-
9	-	-	95.34 ± 0.35	-
10	-	-	98.6 ± 0.43	-

Table 13: Invitro drug release data of F5 to F9 formulations

Time in h	% Cumulative drug release				
	F5±SD	**F6±SD**	**F7±SD**	**F8±SD**	**F9±SD**
0	0	0	0	0	0
1	32.48 ± 0.43	27.60 ± 0.46	33.25 ± 0.23	28.45 ± 0.42	25.43 ± 0.48
2	49.23 ± 0.42	38.40 ± 0.45	47.40 ± 0.42	39.38 ± 0.29	42.47 ± 0.45
3	57.43 ± 0.47	47.48 ± 0.37	60.11 ± 0.19	49.48 ± 0.35	52.52 ± 0.4
4	68.41 ± 0.41	57.46 ± 0.4	71.4 ± 0.29	58.56 ± 0.44	59.58 ± 0.42
5	78.36 ± 0.47	65.4 ± 0.4	80.16 ± 0.22	67.3 ± 0.20	65.23 ± 0.13
6	86.31 ± 0.52	72.44 ± 0.41	88.41 ± 0.25	76.62 ± 0.44	70.52 ± 0.45
7	91.41 ± 0.38	78.53 ± 0.42	93.41 ± 0.35	84.57 ± 0.35	76.43 ± 0.38
8	95.22 ± 0.12	83.84 ± 0.7	98.3 ± 0.39	89.39 ± 0.43	83.54 ± 0.38
9	98.53 ± 0.35	89.17 ± 0.22	-	94.45 ± 0.38	88.37 ± 0.48
10	-	94.43 ± 0.42	-	98.47 ± 0.40	92.45 ± 0.41
11	-	98.35 ± 0.31	-	-	95.5 ± 0.41
12	-	-	-	-	98.38 ± 0.36

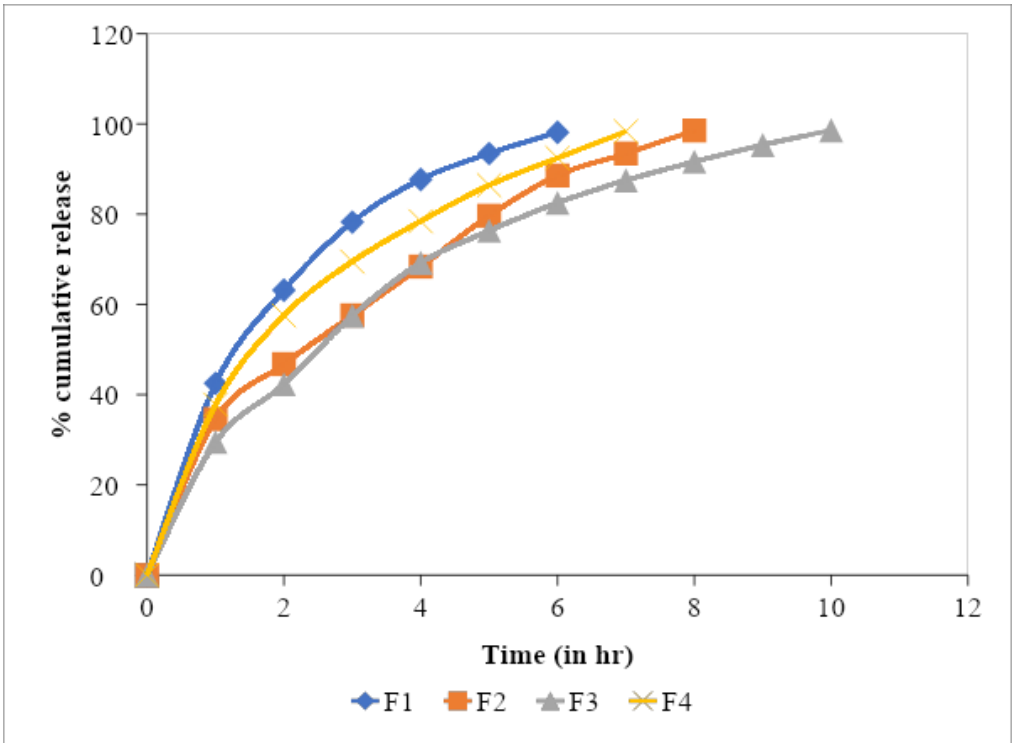

Figure 12: Invitro % cumulative release plot of F1 to F4 formulations

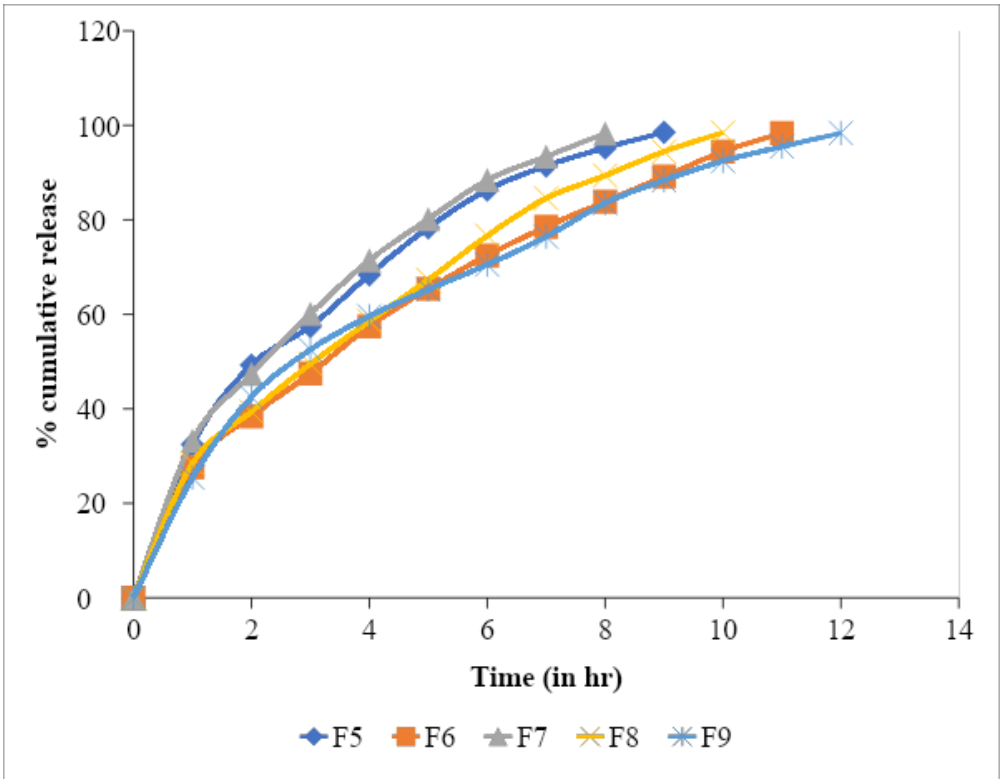

Figure 13: Invitro % cumulative release plot of F5 to F9 formulations

Table 14: Higuchi's data of formulations F1 to F4

Sqrt	% Cumulative medicine release			
	F1 ± SD	F2 ± SD	F3 ± SD	F4 ± SD
0	0	0	0	0
1	42.5 ± 0.40	34.58 ± 0.47	29.52 ± 0.41	37.78 ± 0.32
1.41	63.16 ± 0.23	46.77 ± 0.32	42.34 ± 0.51	57.54 ± 0.42
1.73	78.25 ± 0.29	57.58 ± 0.37	57.46 ± 0.40	69.48 ± 0.33
2.00	87.69 ± 0.50	68.38 ± 0.46	69.22 ± 0.17	78.43 ± 0.49
2.24	93.43 ± 0.31	79.65 ± 0.34	76.32 ± 0.49	86.40 ± 0.27
2.45	98.14 ± 0.18	88.56 ± 0.40	82.52 ± 0.39	92.44 ± 0.38
2.65	-	93.44 ± 0.29	87.5 ± 0.42	98.34 ± 0.32
2.83	-	98.55 ± 0.40	91.62 ± 0.3	-
3.00	-	-	95.34 ± 0.35	-
3.16	-	-	98.6 ± 0.43	-

Table 15: Higuchi's data of formulations F5 to F9

Sqrt	**% Cumulative drug release**				
	F5±SD	**F6±SD**	**F7±SD**	**F8±SD**	**F9±SD**
0	0	0	0	0	0
1	32.48 ± 0.43	27.60 ± 0.46	33.25 ± 0.23	28.45 ± 0.42	25.43 ± 0.48
1.41	49.23 ± 0.42	38.40 ± 0.45	47.40 ± 0.42	39.38 ± 0.29	42.47 ± 0.45
1.73	57.43 ± 0.47	47.48 ± 0.37	60.11 ± 0.19	49.48 ± 0.35	52.52 ± 0.4
2.00	68.41 ± 0.41	57.46 ± 0.4	71.4 ± 0.29	58.56 ± 0.44	59.58 ± 0.42
2.24	78.36 ± 0.47	65.4 ± 0.4	80.16 ± 0.22	67.3 ± 0.20	65.23 ± 0.13
2.45	86.31 ± 0.52	72.44 ± 0.41	88.41 ± 0.25	76.62 ± 0.44	70.52 ± 0.45
2.65	91.41 ± 0.38	78.53 ± 0.42	93.41 ± 0.35	84.57 ± 0.35	76.43 ± 0.38
2.83	95.22 ± 0.12	83.84 ± 0.7	98.3 ± 0.39	89.39 ± 0.43	83.54 ± 0.38
3.00	98.53 ± 0.35	89.17 ± 0.22	-	94.45 ± 0.38	88.37 ± 0.48
3.16	-	94.43 ± 0.42	-	98.47 ± 0.40	92.45 ± 0.41
3.32	-	98.35 ± 0.31	-	-	95.5 ± 0.41
3.46	-	-	-	-	98.38 ± 0.36

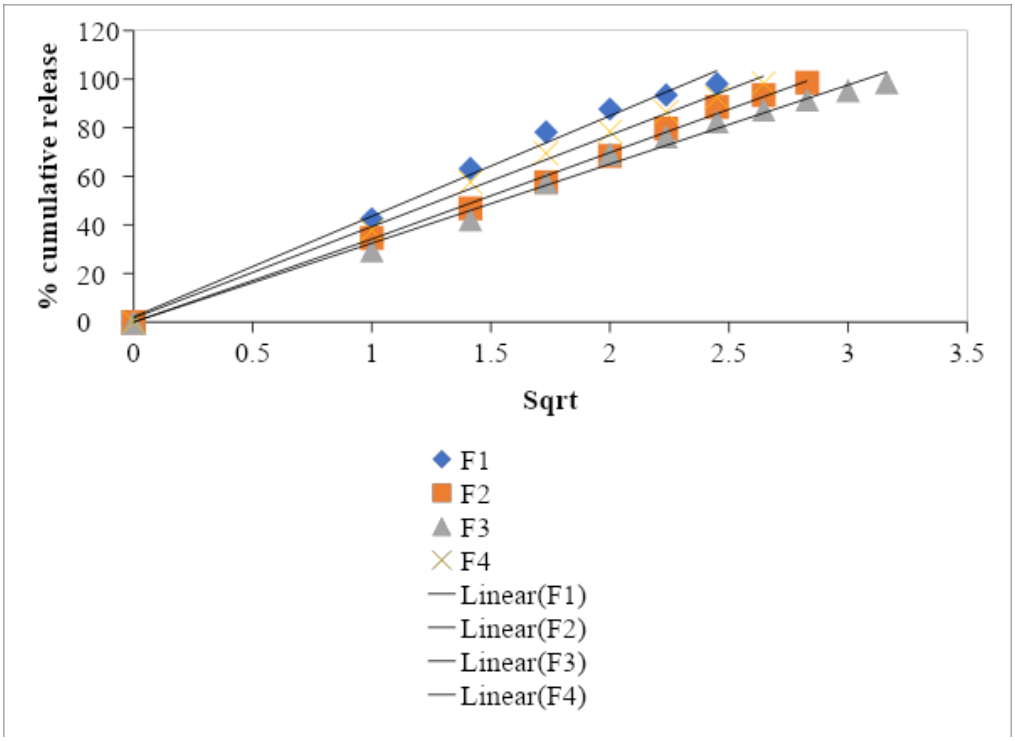

Figure 14: Higuchi's plot for F1toF4 formulations

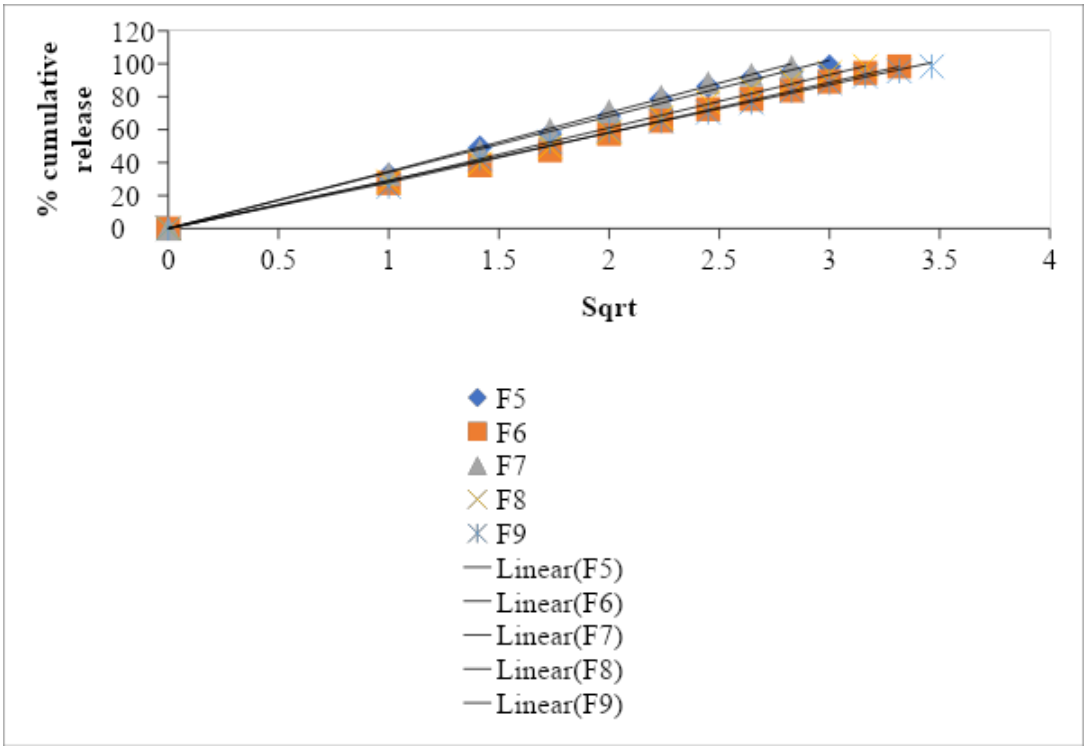

Figure 15: Higuchi's plot of formulations F5 to F9

Table 16: Peppa's data for F1 to F4 formulations

Log time	Log % Cumulative drug release			
	F1±SD	**F2±SD**	**F3±SD**	**F4±SD**
0.000	1.628	1.539	1.470	1.577
0.301	1.800	1.670	1.627	1.760
0.477	1.893	1.760	1.759	1.842
0.602	1.943	1.835	1.840	1.894
0.699	1.970	1.901	1.883	1.937
0.778	1.992	1.947	1.917	1.966
0.845	-	1.971	1.942	1.993
0.903	-	1.994	1.962	-
0.954	-	-	1.979	-
1.000	-	-	1.994	-

Table 17: Peppa's data for F5 to F9formulations

Log time	Log % Cumulative drug release				
	F5 ± SD	**F6 ± SD**	**F7 ± SD**	**F8 ± SD**	**F9± SD**
0.000	1.512	1.441	1.522	1.454	1.405
0.301	1.692	1.584	1.676	1.595	1.628
0.477	1.759	1.677	1.779	1.694	1.720
0.602	1.835	1.759	1.854	1.768	1.775
0.699	1.894	1.816	1.904	1.828	1.814
0.778	1.936	1.860	1.947	1.884	1.848
0.845	1.961	1.895	1.970	1.927	1.883
0.903	1.979	1.923	1.993	1.951	1.922
0.954	1.994	1.950	-	1.975	1.946
1.000	-	1.975	-	1.993	1.966
1.041	-	1.993	-	-	1.980
1.079	-	-	-	-	1.993

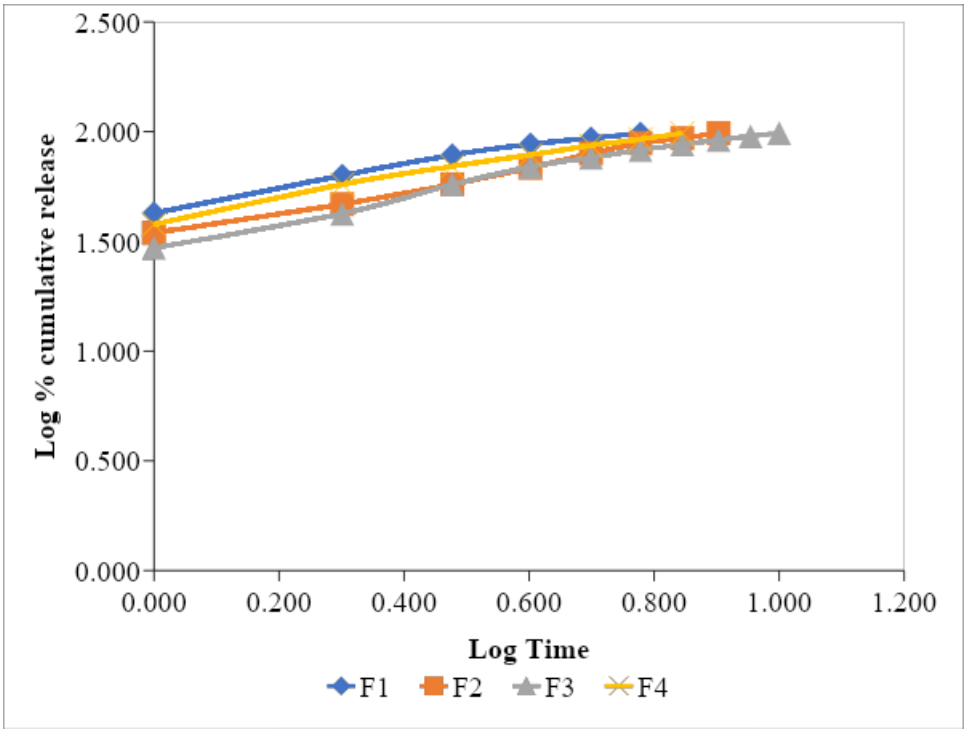

Figure 16: Peppa's plot for F1 to F4 formulations

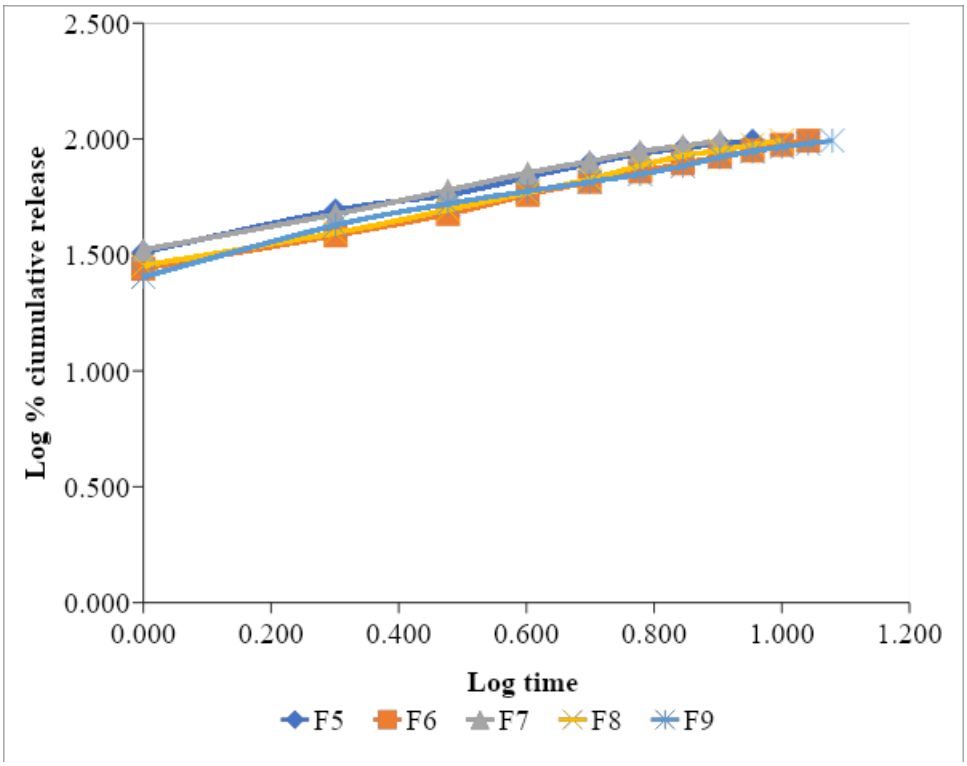

Figure 17: Peppa's plot of formulations F5 to F9

Table 18: Diffusion characteristics of Formulations F1-F9

Formulation no.	Correlation coefficient values(r)		Diffusion exponent value(n)
	Zero Order	Higuchi's Model	
F1	0.929376	0.995235	0.472
F2	0.963228	0.998375	0.524
F3	0.943896	0.995509	0.535
F4	0.939058	0.997878	0.485
F5	0.949809	0.998018	0.512
F6	0.96799	0.998974	0.544
F7	0.958494	0.998954	0.535
F8	0.971315	0.99744	0.561
F9	0.95336	0.99844	0.524

DISCUSSION

Gastro-retentive systems have potential to remain in stomach region for some hours & significantly prolong the GRT of medicines. Prolonged gastric retention improve solubility & bioavailability for medicine are less soluble in a high pH environment reduces medicine waste.

The goal of the study to formulate & characterize floating tablets Rosiglitazone Maleate by wet granulation method with Xanthan gum, HPMC K15M, as polymers, tartaric acid & sodium bicarbonate as gas producing agent and DCP as diluent & finally to performed the stability studies for improved formulation. The tablet prepared by using approved compatible excipients with Rosiglitazone maleate.

SELECTION OF DRUG

In the present study a dosage form containing Rosiglitazone Maleate, tartaric acid, sodium bicarbonate. DCP and different polymers (like HPMC K15M & Xanthan gum) prepared as floating tablets & evaluated. Moreover, rosiglitazone maleate has a very short shelf life (approx. 3 to 4hrs) and solubility decreases increasing physiological pH, which makes Rosiglitazone Maleate as appropriate candidate to formulate the floating dosage form to prolong the GRT.

Drug-polymer interaction study

The drug-polymer interaction study was performed by using DSC & FTIR i.e. by KBr pellet method.

FTIR

FTIR medicine polymers interaction study are shown in figure no. 4 to 8 & reported in table no. 7. It observed that Rosiglitazone Maleate compatible with polymers used in the formulation.

There have no extra peaks observed. so the selected polymers for the formulations found compatible with the Rosiglitazone Maleate & have no physical interaction.

Differential scanning calorimetry

Differential scanning calorimetry allows the quantitative detection of all the process in which energy required/produced (i.e. exothermic or endothermic phase transformations). The thermo grams of Rosiglitazone Maleate & physical mixture of Rosiglitazone Maleate with HPMC K15M & Xanthan gum are presented in figure no. 09 and 10. The Rosiglitazone Maleate showed melting peak at 125.04°C. Peak of Rosiglitazone Maleate 125.04°C presented at the similar position i.e. close to 124.31^0C in the physical mixture of Rosiglitazone Maleate with both HPMC K15M and Xanthan gum. This confirmed the no interaction between Rosiglitazone Maleate and polymers.

Preformulation Parameters

Determination of λ_{max} of Rosiglitazone Maleate

Based on pre-liminary identification test it is concluded that the Rosiglitazone Maleate fulfilled the identification test. By scanning the medicine in U.V spectrophotometer between 200 to 400 nm range, a sharp peak observed at 318.16 nm by using 0.1M HCL solvent. It is concluded that the medicine has max, of 318.16nm (318 nm as per I.P) as showed in figure no. 3.

Preparation of standard calibration curve of Rosiglitazone Maleate

The standard curve of Rosiglitazone Maleate shows that the drug follows Beer's law in the range 5 to 30 g/ml and the equation was generated it was showed figure 3.1 and table 6. Absorbance = 0.012 Conc + 0, was used to calculate the drug content and % CDR of the dosage form.

Evaluation Parameters

Pre- compressional parameters

Flow properties play a significant role in pharmaceuticals specifically in formulation of tablet. The granules bulk density found in the range of 0.442 to 0.578 gm/ml; the granules tapped density found in the range of 0.521 to 0.578 gm/ml, which shown powder is not bulky. The granules angle of repose observed in the range of 20.1^0 to 23.9^0, which show better flow of the granules, the Carr's index observed in the range of 13.82 to 17.80 which indicate that compressibility of the tablet granules is better as reported in table no. 8.

Post-Compression parameters:

Weight variation:

Manufactured tablets evaluated for weight variation & % deviation from the average weight reported in table no. 9 and observed within the prescribed official acceptance limits.

Friability:

The formulations friability observed between 0.359 to 0.678% are reported in table no. 9 & as that of which observed within the IP limit (i.e. NMT 1%).

Tablet hardness & thickness:

The tablet thickness indicates that die filling was uniform. The thickness based upon the punch size (07 mm) and the tablet weight (150 mg). The batch thickness of the formulation F1-F9 found 2.80 to 2.83 mm & hardness found 3.9 to 4.3 Kg/cm^2 as described in table no. 9 which have good mechanical strength.

Medicine content

The medicine content assessment data for all the formulations shown in table 10 found to be within the acceptance limit.

In Vitro Floating studies

Floating Studies performed by using 0.1M HCL solution at 37 pH, the tablets floated & remained floating with-out disintegration. Table no.11 and figure no. 11 showed the results of dissolution study & figure no. 12 showed floating characteristic of set tablet. Duration of set tablet floating of each batch remained float up to 12 hours.

In Vitro dissolution study

In-vitro dissolution studies performed for all the formulations by using USP type-II tablet dissolution apparatus employing handbasket type in 900 ml of 0.1 M HCL as dissolution medium at 50 rpm. The expression F1 formulation containing medicine: HPMC (1:5) shown cumulative % release of 98.14 at 06th hours. But the ideal formulation is developing Rosiglitazone Maleate tablet which sustain the release up to 12 hours. F2 Formulation containing medicine: HPMC (1:6) showed 98.55 cumulative % release at the end of 08th hours. expression F3 formulation containing medicine: HPMC (1:7) was increased showed 98.6 cumulative % release at the end of 10th hours.

In formulation F4, F5, F6 attempt made to achieve the ideal formulation by adding Xanthan gum instead of HPMC. The F4 formulation containing medicine: Xanthan gum (1:5) shown cumulative % release of 98.34 at 7^{th} hour. F5 formulation containing medicine: Xanthan gum (1:6) was increased to sustain the medicine release up to 12 hours, showed 98.47 cumulative % release at the end of 9th hours. F6 formulation containing medicine: Xanthan gum (1:7)

was raise to sustain the release up to 12 hours, showed 98.30 cumulative % release at the end of 11th hours.

An attempt made to improve the release of medicine by using admixture of Xanthan gum & HPMC in different ratio. F7 Formulation containing combination of Xanthan gum: HPMC (1:2) showed cumulative % release of 98.30% at 8^{th} hours. F8 Formulation Xanthan gum: HPMC (1:1) showed 98.30% cumulative medicine release at the end of 10^{th} hours. F9 Formulation containing Xanthan gum: HPMC (2:1) showed 98.38% cumulative medicine release at the end of 12^{th} hours. F9 Formulation found to achieve the main goal.

CONCLUSION

The conception of floating tablets formulation containing RZM offers a appropriate, practical approach to achieve a extended remedial effect by continuously releasing the medicine over the extended time period. In current work, floating tablets of Rosiglitazone Maleate set positively by wet granulation using the different consideration & combination of polymers such as Xanthan gum & HPMC K15-M, , sodium bicarbonate & tartaric acid as gas producing agent, other excipients are similar as DCP as diluent, magnesium stearate as lubricant, talc as glidant & PVP K 30 as a binder. All the Pre-compression parameters like bulk density, tapped density, angle of repose, Carr's index studied. The compressed tablets were subordinated to drug content, friability, hardness, weight variation, in-vitro dissolution studies, floating properties & stability studies. The drug & excipients compatibility was studied by FTIR & DSC which revealed there was no physical or chemical effect. Floating tablets of Rosiglitazone Maleate manufactured by using hydrophilic swellable polymer (HPMC K15M), natural gum (Xanthan gum), tartaric acid, sodium bicarbonate, Mg stearate, talc & DCP by wet granulation method, set up to be good with-out capping, chipping, & sticking. The drug content was uniform in all the tablet formulations, which indicate uniform distribution of drug within the predefined matrix. From in-vitro dissolution studies, it was concluded that all formulation shown acceptable floatation competence & remained floating for more than 12 hrs. In-vitro studies concluded that as attention of polymer i.e. HPMC K15M is increased in Formulation F1, F2, F3 showed a rise in release time up to 06, 08 & 10 hrs independently. formulation with Xanthan gum in F4, F5 & F6 release is found increased up to 07, 09 & 11 hrs independently. With combination of Xanthan gum & HPMC K15 M in formulation F7, F8 & F9 release found increased up to 08, 10, & 12 hrs independently. By SR up to 12 hrs F9 was found to be better formulation. All formulation shown 'n' value in range of 0.45 to 0.89 for Peppas plot indicating that the medicine release by irregular transport (non-fickian diffusion). The stability studies performed for 90 days shown that the

improved formulation (F9) was stable and complete without any degradation. Final improved formulation (F9) was found complying with all properties of tablets & the formulation found acceptable.

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