International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN:2347-6567

IJAMSCR | Volume 8 | Issue 4 | Oct - Dec - 2020
www.ijamscr.com

Research article *Medical research*

Gastro-retentive drug delivery system of rosiglitazone maleate

Dr. Sangeeta Asija[1]*, Bhavana Salunke[2], Dr. Rajesh Asija[3], Mr. Anil Kumar Goyal[4], Mr. Jitendra Kumar[5]

[1*]*Professor & HOD, Swami keshvanand Institute of Pharmacy, Maharishi Arvind Institute of pharmacy, Jaipur, India*
[2] *Student, Maharishi Arvind Institute of pharmacy, Jaipur, India*
[3] *Principal, Maharishi Arvind Institute of pharmacy, Jaipur, India*
[4]*Associate professor, Maharishi Arvind Institute of pharmacy, Jaipur, India*
[5]*Senior Executive, Medicef Pharma, Himachal Pradesh, India*

***Corresponding Author**: **Dr. Sangeeta Asija**
Email id: sangeetaasija@gmail.com

ABSTRACT

Gastro retentive tablets of Rosiglitazone Maleatewere developed to prolong the gastric residence time, leading to an increase in drug bioavailability and reduced dose frequency. Rosiglitazone Maleateis an anti-diabetic agent is used in the management of Type-II diabetes mellitus. The formulated Gastro retentivetablets containing8 mg Rosiglitazone Maleatewere developed using Hydroxyl propyl methyl cellulose (Benecil) and different additives. The formulated tablets obtained by the direct compression method, followed by optimization of the evaluated parameters wereemployed to get the final optimized formulation. The resulting formulations indicated optimum hardness, uniform thickness,consistent weight uniformity and low friability. The formulated tablets were able to continuously float over the stimulatedgastric fluid for 24hrs. The results of *in vitro* drug release studies showed that optimized formulation (PF5) could release the drug (98%) for more than 24 hrs and remain buoyant for more than 24 hrs.

Keywords: Rosiglitazone Maleate, Gastro-retentive Drug Delivery System, Hydroxyl propyl methyl cellulose, Floating Tablet.

INTRODUCTION

GRDDS is an approach to prolong the gastric residence time, thereby aiming site-specific drug release in the upper GIT for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs. Prolonged GRT enables the controlled delivery of drugs in stomach which can evade the repeated administration of dosage form of the drugs with short half-life.[1] Literature suggests that GRDDS has gained huge popularity in the field of oral drug delivery recently, as it can release the drug slowly that can combat many shortcomings allied with conventional oral delivery, including poor bioavailability. Studies demonstrate that the drugs which has to be in the upper part of the GIT, have been prepared as gastroretentive dosage forms using various approaches. Such formulations improve the therapeutic efficacy of the drug and enhance the patient compliance.[2,3]

Rosiglitazone Maleate is an effective oral anti-diabetic agent that belongs to the thiazolidonediones drug class and is widely prescribed in the management of non-insulin dependent (Type II) diabetes mellitus. It is poorly soluble in aqueous fluids and is majorly absorbed from stomach. Dosage forms that are retained in the stomach would increase its oral bioavailability and efficacy. Rosiglitazone Maleate has a short biological half-life and is eliminated rapidly. So the Gastro retentive floating tablet formulations are needed for Rosiglitazone Maleate to prolong its duration of action and to increase its oral bioavailability and to improve patient compliance.[4,5]

Therefore, in the present study it was aimed to design gastroretentive floating tablets of Rosiglitazone Maleate by using Benecil K100M polymers as tablet matrix formers and sodium bicarbonate as gas generating agent.[6]

MATERIALS AND METHODS

Materials

Gift sample of Rosiglitazone Maleatewas received fromas giftsample from Syskem Pharmocrats, Solan, BenecilK100M, sodium bicarbonate (NaHCO3), Citric acid, Microcrystalline cellulose, mag. stearate, talc, were received fromSignet., Mumbai.

Drug-excipient compatibility studies

To study the compatibility of various formulation excipients with Rosiglitazone Maleatesolid admixtures were prepared by mixing the drug with each formulation excipient separately in the ratio of 1:1 and stored in air tight containers. The solid admixtures were characterized using Fourier transform infrared spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC)[7].

Preparation of standard curve of Rosiglitazone Maleate

An accurately weighed amount of Rosiglitazone Maleate was transferred into a 100 ml volumetric flask containing 0.1N HCl to dissolve and then the volume was made up to the mark with 0.1N HCl. From this stock solution necessary dilutions were made to give solutions with concentrations ranging from 0-35 µg/ml. The absorbances of the volumetric solutions were recorded at 318 nm.[8]

Formulation of Rosiglitazone Maleate floating matrix tablets

Tablets containing 8.0 mg Rosiglitazone Maleate were prepared by direct compression. The respective powders, namely Rosiglitazone Maleate, release retarding polymer viz. (Benecil), a gas generating agent ($NaHCO_3$) were passed through sieve no.60 separately. Mixing of powders was carried out using a mortar & pestle for 10 min, then other ingredients viz. citric acid and microcrystalline cellulose were added in geometric proportions, and all these were mixed homogenously and then lubricated with the previously weighed and sieved magnesium stearate, talc in a polybag for about 5-10 min, to obtain the blend for compression. Finally, 300 mg of each mixture was compressed on sixteen station rotary tablet punching machine having 10 mm punches to produce the desired tablets.[9]

Table 1.0: Composition of floating tablet of Rosiglitazone Maleate

Ingredients	Quantity (mg)								
	PF1	**PF2**	**PF3**	**PF4**	**PF5**	**PF6**	**PF7**	**PF8**	**PF9**
Drug	8	8	8	8	8	8	8	8	8
Benecil K100M	30	60	90	30	60	90	30	60	90
Sodium Bicarbonate	30	30	30	45	45	45	60	60	60
Citric acid	10	10	10	10	10	10	10	10	10
Avicel	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg	q. s. to 300 mg
Mg stearate	2	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4	4
Total weight	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**

Evaluation parameters of the tablet Physical characterization[10,11]

Tablet thickness

A Vernier calipers (Make: DigimaticMitutoyo) was used to determine thickness of 10 randomly selected tablets. Five tablets of each formulation were taken randomly and thickness was measured individually

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Five tablets were randomly picked and hardness of the tablet was determined.

Weight variation test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. Twenty tablets were randomly selected and accurately weighed, in grams on an analytical balance

Friability Test

According to the BP specifications 10 tablets were randomly selected and placed in the drum of a tablet friability test apparatus (Electrolab, India). The drum was adjusted to rotate 100 times in 4 min. the tablets were removed, dedusted and accurately weighed. The percent weight loss was calculated.

Drug content uniformity

Ten tablets were individually weighed, crushed and quantity of powder equivalent to the mass of one tablet (300 mg) was extracted in 100 ml of 0.1N HCl. The solution was filtered through a cellulose acetate membrane (0.45 µm). The drug content was determined by UV spectroscopy (double beam spectrophotometer, Shimadzu, Kyoto, Japan) at a wavelength 318 nm after a suitable dilution with 0.1N HCl.

Determination of swelling index

The swelling behavior of the tablets was determined in triplicate, according to the method, a tablet was weighed (W1) and placed in a glass beaker, containing 200ml of 0.1N HCl, maintained in a water bath at 37 ± 0.5°C. At regular intervals, the tablets were removed & the excess surface liquid was carefully removed by a filter paper. The swollen tablet was then reweighed (W2). The swelling index [SI] was calculated using the formula.

SI= (W2-W1) / W1

Tablet Floating behavior

The floating behavior of the tablets was visually determined, in triplicate, according to the floating lag time method, a tablet was placed in a glass beaker, containing 200ml of 0.1N HCl, maintained in a water bath at 37±0.5°C. The floating lag time "the time between tablet introduction & its buoyancy" and total floating duration "the time during which tablet remains buoyant" were recorded.

Drug release studies

Drug release studies of the prepared floating tablets were performed in triplicate, in a USP Dissolution Apparatus, type II (Paddle method) (Electrolab India) at 37±0.5°C. The paddles rotated at a speed of 100 rpm. The tablets were placed into 900 ml of 0.1N HCl solution (pH 1.2). Aliquots of 5ml were withdrawn from the dissolution apparatus at different time intervals & filtered through a cellulose acetate membrane (0.45µm). The drug content was determined spectrophotometrically at a wavelength of 318. At each time of withdrawal, 5ml of fresh medium was replaced into dissolution flask.

RESULTS AND DISCUSSION

Compatibility Study

The drug & polymers were characterized byFourier transformed infrared spectroscopicanalysis (FT-IR), to ascertain for any interactionbetween the drug and the polymers used and toconfirm the encapsulation of the drug with inpolymer matrix. For this purpose, spectra of thepure drug, and mixture containing the drug andpolymer was taken. An FT-IR spectrometer was used for the analysis in the frequency rangebetween 4000 to 500 cm^{1}. No significant change occurred in the characteristics peaks of Rosiglitazone Maleate in all the solid admixtures. The spectrum shown in (Figures 1,2).

The DSC spectra of Rosiglitazone Maleate solid admixtures of drug and excipients were recorded at the temp range upto 300ºC. Characteristics peaks of Rosiglitazone Maleate at 196ºC were observed. The spectrum shown in (Figures 3,4).

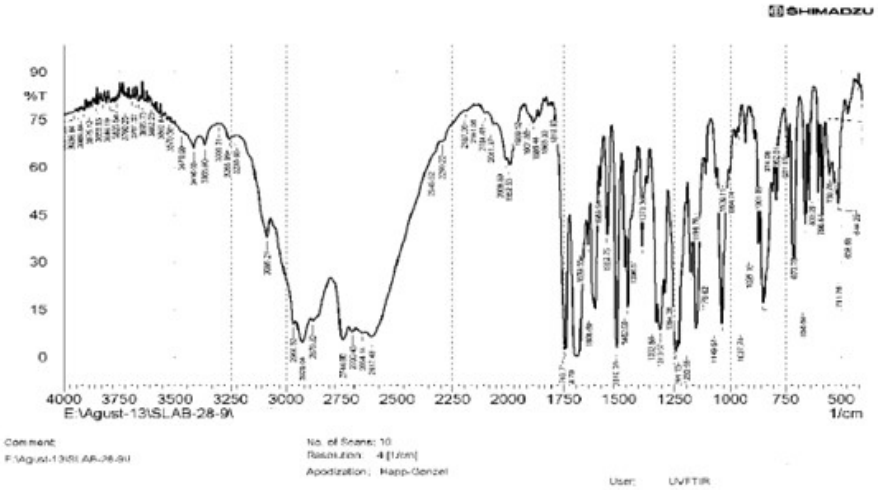

Fig. No.1: FTIR Spectra of Rosiglitazone Maleate Pure Drug

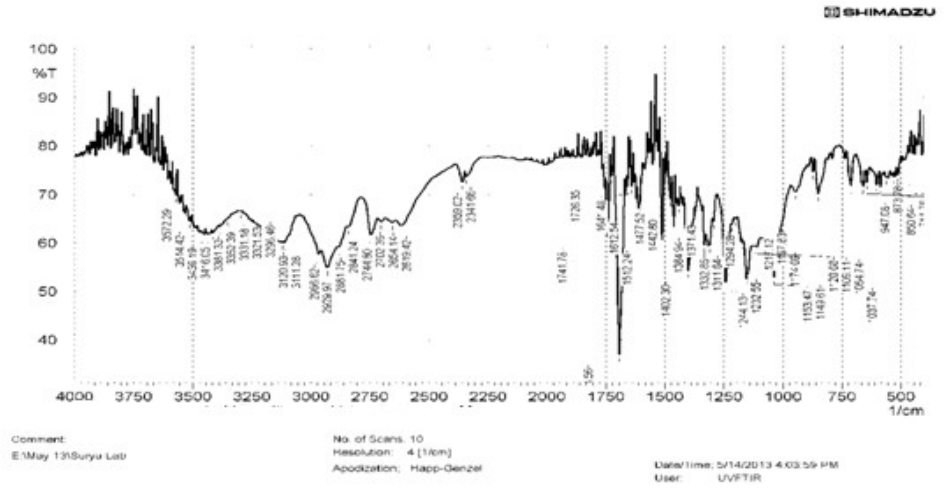

Fig. No.2: FTIR Spectra of Rosiglitazone Maleate and Benecil K100M

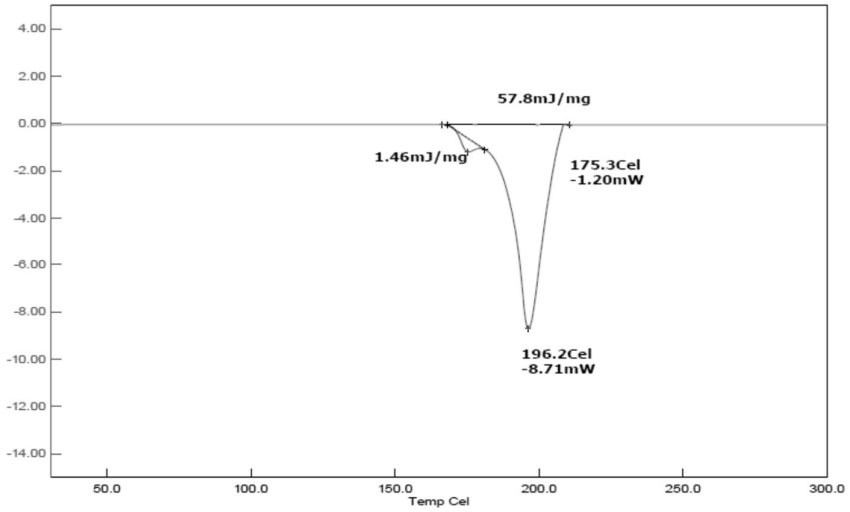

Fig. No.3: DSC Thermogram of Rosiglitazone Maleate Pure Drug

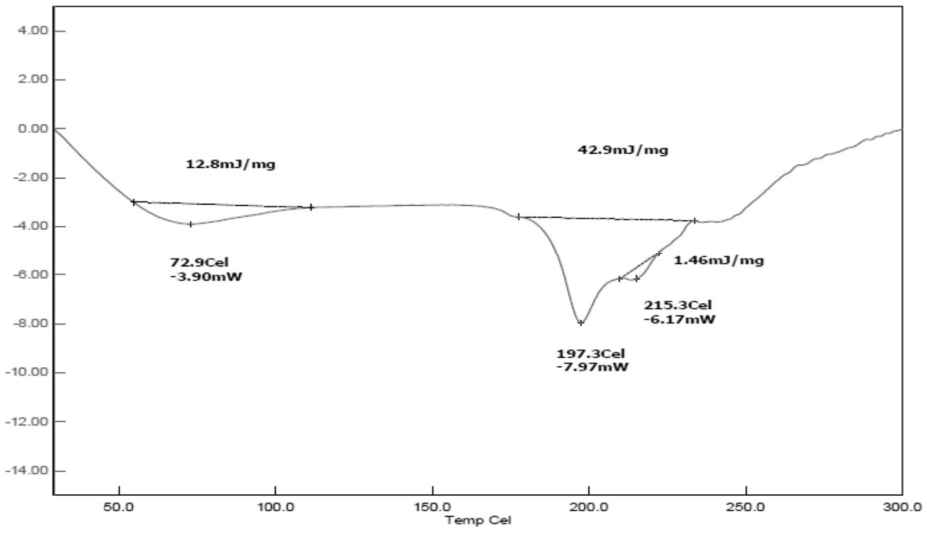

Fig. No.4: DSC Thermogram of Rosiglitazone Maleate + Benecil K100

Standard curve of Rosiglitazone Maleate

Table 2.0: Standard graph of Rosiglitazone Maleate in 0.1N HCl

Concentration (µg/ml)	Absorbance at 318 nm
0	0
5	0.151
10	0.273
15	0.421
20	0.565
25	0.688
30	0.815
35	0.951

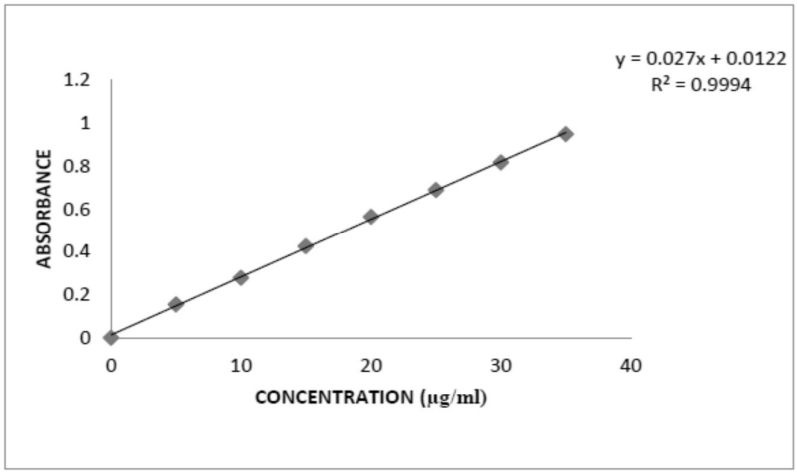

Fig. No.5: Standard Curve of Rosiglitazone Maleate in 0.1N HCl

Physical Evaluation of tablets

The formulated tablets were subjected forvarious evaluation parameters like hardness,thickness, weight variation, friability, Floating time and Swelling Index. Our experimentalresults (Table 3) revealed that all the formulatedtablets were of good quality with regard to hardness (4.5 to 5.0 kg/cm2), friability (below 1%) andthickness (4.22 to 4.43 mm). The weight variationof the tablet in the range is below 5%, complying with pharmacopoeialspecification. From the results all batches showsgood floating (up to 24 hours).

Drug Content

Drug content was determined by using equationprepared from the Calibration curve of theRosiglitazone maleate in 0.1 N HCl and calculated by using equation (Y=0.027X+0.0122).The percentage of drug content was found to be between 97.34 to 102.11 which was within acceptable limits. Table no3, showed the result of drug content uniformity in each batch.

In vitro dissolution studies

Depending on the type and concentration of the polymer, variable drug release profiles were successfully tailored. The influence of the polymers and sodium bicarbonate concentration on the release of Rosiglitazone Maleate from the floating tablets in 0.1N HCl (pH 1.2) at 37 ± 0.5˚ C is clearly seen in fig. no. 5, 6, and 7. It is clear that the formulas prepared succeeded in controlling the rate of drug release for 24 hr as shown in table 6.

Under identical experimental conditions, the cumulative % drug release of formulae PF2, PF5, PF8 (Benecil K 100M), with 20% polymer concentration and 10%, 15% and 20% w/w ($NaHCO_3$) concentration with each polymer, has shown 54.96%, 59.40%, 68.40% (BenecilK 100M), cumulative % drug release at the end of 12 hrs respectively. Similarly PF3, PF6, PF9 (Benecil K 100M), formulae with 30% polymer concentration and incremental concentration of $NaHCO_3$as mentioned above showed cumulative % drug release of 43.50%, 48.60%, 50.20% (Benecil K100M) respectively at end of 12 hrs.

From the pattern of the drug release it is clear that the degree of retardation of the drug release rate from the formulae PF1 to PF9 was a function of polymer concentration.

Table 3.0: Results of physical parameters of Rosiglitazone Maleatefloating matrix tablets

Formulations	Tablet weight (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Content uniformity (%)
PF1	303	4.62	4.30	0.30	98.23
PF2	296	4.54	4.26	0.20	102.11
PF3	287	5.00	4.29	0.50	99.12
PF4	300	4.98	4.41	0.35	98.76
PF5	293	5.00	4.31	0.29	101.76
PF6	304	4.76	4.22	0.10	99.54
PF7	292	5.01	4.28	0.27	97.34
PF8	307	4.97	4.40	0.12	98.46
PF9	296	4.56	4.43	0.20	101.56

Table 4.0: Floating lag time and Total floating time of Rosiglitazone Maleate

Formulations	Floating lag time (sec)	Total floating time (hrs)
PF1	36	24
PF2	54	24
PF3	73	24
PF4	24	24
PF5	45	24
PF6	63	24
PF7	15	24
PF8	34	24
PF9	49	24

Table 5.0: Time swelling index studies of Rosiglitazone Maleate

Time (hrs)	Swelling index (%)								
	Formulations								
	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9
1	25.60	40.15	49.56	29.25	44.56	54.56	33.63	47.75	59.55
2	39.65	52.17	63.56	42.66	56.60	66.65	46.26	59.69	70.56
4	74.25	86.59	91.55	78.20	89.45	95.92	81.17	93.57	98.99
6	87.65	94.17	102.78	90.80	97.78	106.73	94.59	100.95	115.16
8	99.50	110.50	121.26	108.56	116.89	127.44	112.60	123.55	135.60

Table 6.0: Results of dissolution studies of Rosiglitazone Maleate

Formulations	% DRUG RELEASE									
	1hr	2hr	3hr	4hr	6hr	8hr	10hr	12hr	20hr	24hr
PF1	31.23	40.53	47.20	55.50	68.88	75.53	81.63	87.30	98.45	99.00
PF2	20.44	22.77	27.21	30.43	35.10	40.83	47.20	54.96	91.90	99.00
PF3	15.75	18.30	19.43	24.30	26.10	33.06	39.96	43.50	64.96	76.10
PF4	34.43	39.00	44.30	49.44	54.53	67.77	74.93	90.53	98.90	99.00
PF5	19.43	26.63	32.53	38.63	44.73	47.86	51.46	59.40	90.5	99.00
PF6	19.96	23.40	27.30	31.20	35.30	39.53	45.73	48.60	66.20	77.53
PF7	39.06	43.43	50.10	54.30	62.63	71.40	79.76	91.50	98.80	99.00
PF8	15.06	30.63	36.20	43.43	47.40	49.83	58.43	68.40	92.30	99.00
PF9	18.73	24.40	26.40	31.96	37.30	40.43	43.50	50.20	69.73	82.50

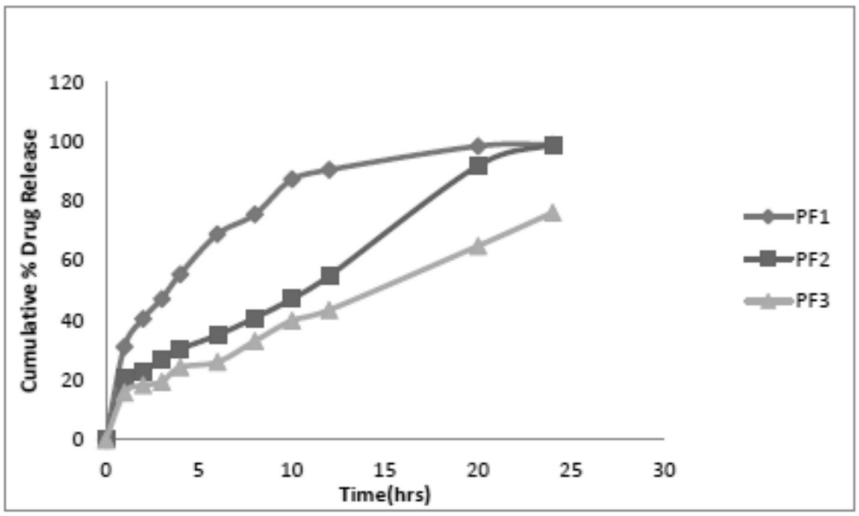

Fig. No.6: Release profiles of Rosiglitazone Maleatefrom floating matrix tablets

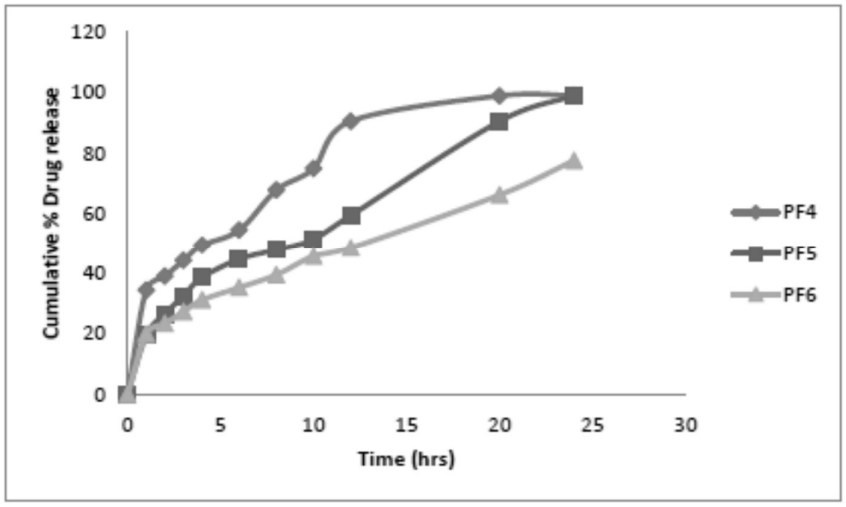

Fig. No.7: Release profiles of Rosiglitazone Maleatefrom floating matrix tablets

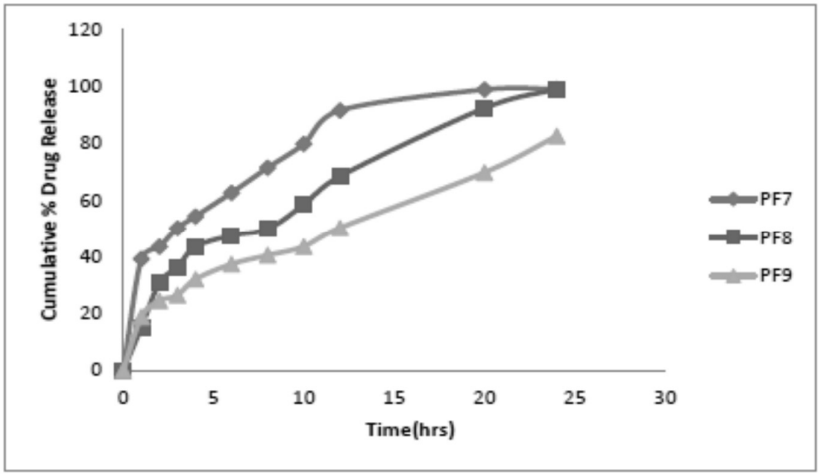

Fig. No.8: Release profiles of Rosiglitazone Maleatefrom floating matrix tablets

CONCLUSION

Observations of all formulations for physicalcharacterization had shown that, all of themcomply with the specifications of officialpharmacopoeia and/or standard reference.Drug & excipients compatibilities were carried outby using FTIR& DSC, which showed no significantchange in any way to the mixture. Tablets were evaluated forweight variations, hardness, friability, thickness,and Floating studies. Release studies werecarried out in 0.1 N HCL, for 24 hours. Based on all the observations and results, it is revealed that the Rosiglitazone Maleate floating tablets prepared by employing PF5was the best formulation.

REFERENCES

1. Gupta, N.V. and Shivakumar, H.G., Preparation and characterization of superporous hydrogels as gastroretentive drug delivery system for rosiglitazone maleate. DARU Journal of Pharmaceutical Sciences, 2019.18(3).
2. Dorożyński, P., Kulinowski, P., Mendyk, A. and Jachowicz, R. Gastroretentive drug delivery systems with l-dopa based on carrageenans and hydroxypropylmethylcellulose. International Journal of Pharmaceutics, 2019, 404(1).
3. Jain, V. and Singh, R., Design and characterization of colon-specific drug delivery system containing paracetamol microsponges. Archives of Pharmaceutical Research, 2018, 34(5).
4. Gambhire, M.N., Ambade, K.W., Kurmi, S.D., Kadam, V.J. and Jadhav, K.R., Development and in vitro evaluation of an oral floating matrix tablet formulation of diltiazem hydrochloride. AAPS PharmSciTech, 2017.8(3).
5. Basak, S.C., Rao, K.N., Manavalan, R. and Rao, P.R., Development and in vitro evaluation of an oral floating matrix tablet formulation of ciprofloxacin. Indian Journal of Pharmaceutical Sciences, 2017. 66(3).
6. Asnaashari, S., Khoei, N.S., Zarrintan, M.H., Adibkia, K. and Javadzadeh, Y., Preparation and evaluation of novel metronidazole sustained release and floating matrix tablets. Pharmaceutical Development and Technology, 2015. 16(4).
7. Anamika Saxena, Kaplesh Gaur, Virender Singh, Rajneesh Kanth singh and Ashok Dashora. Floating microspheres as drug delivery system. AJPPS, 2014; 1, 2, 27-36.
8. Sunil Kumar, M Das, K S Gupta, R Kumar, A Chongdar, L K Ghosh. Design, development, optimization and evaluation of Gastroretentive floating tablets of Atenolol. Der Pharmacia letter., 2013; 5, 3, 436-456.
9. Chabria Neetu B, N Narayana, Hygeia. Formulation & in vitro evaluation of oral floating Nicardipine HCl tablets. J.D.Med., 2013; 5, 2, 63-75.
10. Prasad K lende, M S Junajete, Arundhati D Deshmukh. Formulation optimization & in vitro evaluation of floating tablets of Stavudine. Am. J. Pharmatech Res., 2012; 2, 5, 723-739.

How to cite this article: Dr. Sangeeta Asija, Bhavana Salunke, Dr. Rajesh Asija, Mr. Anil Kumar Goyal, Mr. Jitendra Kumar. Gastro-retentive drug delivery system of rosiglitazone maleate. Int J of Allied Med Sci and Clin Res 2020; 8(4): 752-759.

Source of Support: Nil. **Conflict of Interest:** None declared.