

To Formulation and Evaluation of Floating Tablet of Rosiglitazone

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Abstract

In this present study, floating mucoadhesive tablets of Rosiglitazone were formulated to ameliorate the gastric retention time and overall bioavailability. Different mucoadhesive polymers like HPMC K200 M, Na CMC, Carbopol 974P, Karaya goo, Chitosan and Xanthan goo were named to formulate the tablets. colorful phrasings were prepared by using these polymers in different attention. The pre-compression mix of Rosiglitazone mucoadhesive tablets were characterized with respect to angle of repose, bulk viscosity, tapped viscosity, carr's indicator and hausner's rate and all the results indicated that the mix was having good inflow property and hence better contraction parcels. The swelling studies were performed for the phrasings and the results depicted that all the phrasings have a good lump indicator. The medicine release studies depicted that the phrasings release the medicine in first order. So grounded on the results, expression RF13 was set up to be an optimized expression.

Keywords: Mucoadhesive tablets, Rosiglitazone, Bioadhesive polymers

Introduction

Oral Medicine delivery system having major advantages over others because it delivers the medicine in an applicable station to the systemic rotation which leads to patient compliance. also, it has been observed that transcendence figures of medicines are chosen in the oral route than others, nearly 90 of medicines are ideal by this route. Under the marquee of the oral medicine delivery system, there are substantial divisions are available to carry the medicine into the systemic rotation. Bioavailability of medicines in the systemic rotation is veritably smaller in the case of conventional oral medicine delivery due to its reduced hearthstone or slighter preface to the point of immersion window which leads to lower bioavailability. In comparison to the conventional oral medicine delivery system with oral controlled lozenge form systems denote further advantages and overcome problems associated with it. Control medicine delivery systems proved to be more able and profitable than the conventional medicine delivery system because of its perpetual or adaptable release rate.

Merit of GRDDS

- Upsurges Bioavailability of drug elements.

- Due to a definite area of drug delivery cuts objectionable properties.
- It helps to lessen the variation of drug absorptions and adverse properties.
- It up surges the residence period in the abdominal area and lessens the dosing frequency.
- It is more beneficial to the elements that have a shorter half-life.
- It is also known as a primarily site-specific delivery system, due to increase residence time in the abdominal area.
- The due upsurge in residence time in the stomach helps drug elements who have a lesser amount of solubility at a basic pH environment.
- It is more valuable over the conventional system since it over comes the problem allied with.

- **Demerits of GRDDS**

- The release pattern may vary.
- Various factors may alter the release rate of drugs i.e. diet and the rate of passage through gut.
- Release patterns may vary from one formulation to another due to changes in additives.
- Due to loss of reliability in dosage form the availability of loading dose may cause toxicity.
- For such kind of dosage form, it cannot be modified or redesigned.
- Acid labile drugs cannot be given by this route.

- **Different GRDDS dosage form**

- Floating microspheres contain a different category of the drug-like - HMG-CoA reductase inhibitors, Antihypertensive, Antidiabetic, and Antibiotic.
- Floating granule contains a different category of a drug like - Analgesic, ibuprofen, HMG- CoA reductase inhibitors, Antihistamine, and Antihypertensive.
- Films contain different drug category like-Antihistamine
- Floating capsules contain a different category of a drug like- COX-2 inhibitor, Antidiabetic, Antidepressant, Diuretic, and Anti-inflammatory.
- Floating tablets contain a different category of a drug like Antibiotic, Antidiabetic, Antihypertensive, HMG-CoA reductase inhibitors.

- **Application Enhanced bioavailability**

‘Bioavailability’ enhancement is possible for the drugs that are having a narrow absorption window in the stomach. Due to escalation in the residence time of dosage form, the drug can expose to the gastric environment for more period hence the absorption of the drug also improved. It has been proved by comparing with conventional dosage form with drug riboflavin

a. Sustained drug delivery

There are many problems associated with controlled release dosage form which can be minimized by a floating drug delivery system. The major problem associated with a controlled release dosage form is the residence time of formulation in the stomach. By the different approaches of GRDDS this problem can be resolved like- low-density formulation, the larger size of formulation, gas generating, and swelling of formulation techniques

b. Site-specific drug delivery

These frameworks are especially profitable for drugs which precisely engrossed from the 'stomach' or the 'proximal portion' of the digestive system. The primary part of medicaments is absorbed in the abdominal area followed by in duodenum. It has been accounted for dosage forms designed with delayed gastric living arrangement time was shaped and the bioavailability was expanded for furosemide and observed that AUC changed dramatically

- **Absorption**

Medications that have deprived 'bioavailability' in light of site-explicit ingestion from the superior segment of the gastrointestinal plot are expected contender for GRDDS to achieve better absorption by increasing their retention at the spot of absorption. 'A significant increase in the Bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric-coated LASIX-long product (29.5%)'

- **Mechanism of floating systems**

Although the framework is floating on the gastric substance the medication is delivered gradually at the ideal proportion from it. The framework will be exhausted from the stomach after discharging the medicaments from the dosage form. Along with the gastric content, some additional attainments are required for buoyancy like-Force (gravity, acceleration, and vertical)

and volume of fluid. A negligible degree of floating force (F) is additionally needed to retain the dose structure remain float on the supper. To understand the theory behind this it is necessary to measure the vertical force required to float the object. Greater the F value better the floating time

- **Material & Method**

Name of the Chemical
Rosiglitazone
Hydroxypropylmethylcellulose
Sodium Carboxymethyl Cellulose
Carbopol 974P
Karaya Gum
Chitosan
Xanthan Gum
Sodium Bicarbonate
Magnesium Stearate
Talc
Lactose

Table: List of Chemicals

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Name of the Equipment
UV-Visible spectrophotometer
Bulk Density Apparatus
Rotary Punching Machine (Lab Press, India).
Weight Balance
Digital Vernier caliper
Monsanto hardness tester
Roche Friabilator
USP Type II dissolution test apparatus

Table: List of Equipment

• **Preparation Calibration Curve of Rosiglitazone**

For the calibration curve stock solution-I was prepared by dissolving 100mg rosiglitazone and 100 ml of methanol 10 ml of the above arrangement was taken and made up to 100 ml by utilizing 0.1 N HCl (100µg/ml) called as stock solution-II. In the same way, again 10ml solution was withdrawn from stock solution-II and diluted up to 100ml with 0.1N HCl ((10µg/ml) and named as stock solution-III. Followed by the stock solution III was mixed with 0.1 NHCl to maintain the concentration levels as 10, 20, 30, 40, and 50µg/ml of rosiglitazone ml of solution. The obtained series were scanned at 248 nm by utilizing a ‘UV- Spectrophotometer’ with 0.1 NHCl as blank. The obtained absorbance was placed in a graph by taking Concentration on X-Axis and Absorbance on Y-Axis to determine the square of the correlation coefficient (R^2).

➤ **Pre-formulation Studies:**

Pre-formulation studies express about the physicochemical properties of excipients. Excipients having a key role in formulation development, which guides us to select appropriate dosage form and also support to create an outline for the manufacturing.

➤ **Solubility Studies**

The solubility of Rosiglitazone, was figure out in 0.1 N HCl solution. A supersaturation was prepared by mixing medicament and 10ml of solvent in a 20ml vial and sealed it. Sealed vials were placed on the rotary shaker for continuous agitation for a period of 24hrs. at room temperature. As the time over for mixing, the filtrate were passed through 0.2 µm ‘Whatmann’s filter paper’ followed by scanned utilizing ‘UV spectrophotometer’ at 248 nm.

➤ **Preparation of Floating Mucoadhesive Tablets**

The direct compression method is opted to formulate Floating mucoadhesive tablets containing Rosiglitazone trials were developed by altering the proportion of HPMC K200M, Na CMC, Carbopol 974P, Karaya gum, Chitosan, and Xanthan gum. Sodium bicarbonate is helped to float the tablets. Talc and magnesium stearate and lactose are used for enhancing lubrication property, gliding property, and diluent subsequently. The drug, polymers, sodium bicarbonate, and lactose were mixed properly for 15 min until formed a homogeneous mixture. Followed by talc and Magnesium Stearate are added as lubricating agents. The above powder mixture was mixed homogeneously by using a polyethylene bag. Finally, the tablets were prepared by a 6-millimeter width to die in a 9- station pharmaceutical tablet press (Lab Press, India)

Ingredients	RF1	RF2	RF3	RF4	RF5
Rosiglitazone	100	100	100	100	100
HPMC K200M	80	100	120	80	100
NaCMC	-	-	-	-	-
Carbopol 974P	-	-	-	-	-
Karayagum	-	-	-	-	-
Chitosan	-	-	-	-	-
Bees Wax	100	100	100	100	100
NaHCO ₃	50	50	50	50	50
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5
Lactose	60	40	20	60	40
Total Weight (mg)	400	400	400	400	400

Table: The composition of Floating Mucoadhesive tablets of Rosiglitazone

- **Material & Method**

Evaluation Parameters

➤ **Post-compression Evaluation:**

Physicochemical characterization of tablets

The prepared formulation containing different drugs were evaluated for various pre- compression parameters as mentioned below:

- **Weight Variation**

This ‘weight variation’ test is carried out by a random selection of 20 tablets and followed by weighed accurately. The mean weight of 20 tablets calculated and followed by compared with the weight of the tablet individually. If two or more than two tablets are coming outside the range ($\pm 7.5\%$) than it batch is failed or else pass. The same study was repeated to determine the mean (n=3). The percentage of deviation was calculated as follows:

$$\% \text{Deviation} = (\text{Individual weight} - \text{Mean weight} / \text{Mean weight}) \times 100$$

- **Tablet Thickness**

From the production level, the physical shape (external measurement) for the prepared formulation was monitored properly. Various parameters have an impact on thickness like compression force, the shape of the die, and the rotation of machine per minute (RPM) of the compression machine. Hence these criteria are important for the acceptance of formulation, tablet uniformity, and packaging. The Digital Vernier caliper was utilized to examine the physical shape of the tablets. The tablets (10 tablets from a single batch) were selected randomly to find out the average weight. The standard deviation for thickness was calculated.

- **Tablet Hardness**

The hardness of a dosage form explains as a force necessitates / adequate to break it in two parallel plates. Tablets need strong resistance power for additional mechanical shocks. Every batch of tablets was taken (6 tablets) and mechanical strength was estimated by ‘Monsanto hardness tester’ and the mean was calculated. It is expressed in Kg/cm².

- **Friability**

The hardness of a tablet is not sufficient to express the resistance due to loosening their crown positions during compression. Accordingly to cross-check the strength of the table to their measurements for the tablet were proposed i.e. friability (Roche friabilator). A set of tablets that were selected for the test is to get the mechanical force (shock and abrasion). Roche friabilator, with a rotation speed of 25 rpm speed for four minutes.

The underlying load of tablets was noted down before the test. After the test, the tablets were then de-dusted and rechecked. Finally expressed as a percentage of friability.

$$\text{Friability}(\%) = \frac{\text{Initial weight of 10 tablets (W}_0\text{)} - \text{final weight of 10 tablets (W)}}{\text{Initial weight of 10 tablets (W}_0\text{)}} \times 100$$

The initial weight of 10 tablets (W₀)

- **Content of Uniformity**

Randomized selection of formulation (6 Tablet for each formulation) was taken to find out the percentage of pharmaceutical medicaments available in each formulation. Equivalent to the weight of each formulation, the powder was taken and dissolved in 100 ml of 0.1 N HCl by rousing for 10 min. The membrane filter (0.45 μ) was used for straining the above solution and diluted suitably followed by scanned by using a 'UV-Visible spectrophotometer at 248 nm

- **In-vitro Buoyancy studies**

It mainly reflects two parameters i.e. 'Floating lag time' and 'Total floating time'. These two parameters were found out by putting formulation in 0.1N HCl. The 'Floating Lag Time' (FLT) is denoting as a time span for the formulation to reach the top of the medium and the 'Total Floating Time' (TFT) was noted by noting down the extent of floating time

- **In vitro release studies:**

The USP type II testing apparatus was taken for the dissolution study. In Floating mucoadhesive tablets were release the medicaments from a single surface, so to maintain an *in vitro* gastric condition the formulation was partially covered by an impermeable membrane and followed by it was adhered to a glass slide (2x2 cm) 'Cyanoacrylate adhesive'. Then arrangement was positioned in

the 900 ml of pH 1.2 HCl solutions and with a paddle speed 50 rpm at a temperature of 37 ± 0.5 °C. A measured amount of test solution introverted at a fixed duration of spell to 12hrs and scanned by spectra at 248 nm after appropriate dilution

➤ **Result and Discussion**

• **Determination of Absorption Maxima:**

The ‘Standard curve’ depends on the ‘Spectrophotometry’. The maximum absorption was observed at ‘248 nm

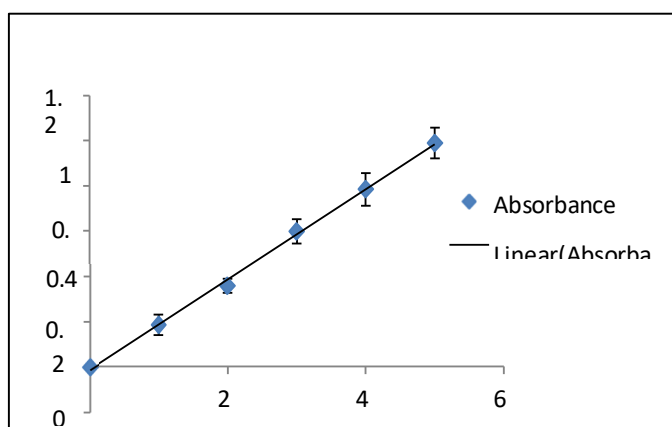


Figure: Rosiglitazone in 0.1N HCl

S. No	Concentration (µg/mL)	Absorbance
1	0	0 ± 0
2	10	0.185 ± 0.045
3	20	0.358 ± 0.031
4	30	0.598 ± 0.053
5	40	0.784 ± 0.072
6	50	0.989 ± 0.068

Table: Calibration curved at a for Rosiglitazone

➤ **Pre-formulation Studies**

- Solubility Studies

Table: Solubility studies Rosiglitazone

S. No	Medium	Amount present (µg/mL)
1	Water	30.67
2	Methanol	100.98
3	0.1 N HCl	48.82

- **Characterization of Pre-Compression Blend**

Table: Results for Derived and Flow properties of Rosiglitazone

Formulation Code	Derived properties		Flow properties		
	Bulk density (mean ± SD)	Tapped density (mean ± SD)	Angle of repose (mean ± SD)	Carr's index (mean ± SD)	Hausner's Ratio (mean ± SD)
RF1	0.416±0.009	0.476± 0.008	26.7 ±0.47	12.50± 0.35	1.14± 0.34
RF2	0.384± 0.007	0.434± 0.006	26.0 ±0.34	11.53± 0.25	1.13± 0.28
RF3	0.555± 0.011	0.714± 0.013	26.6 ±0.22	22.22± 0.15	1.28± 0.36
RF4	0.384± 0.004	0.441± 0.006	25.98±0.40	13.46± 0.19	1.15± 0.27
RF5	0.266± 0.013	0.312± 0.017	26.32±0.87	14.66± 0.27	1.16± 0.39

Note: Each worth speaks to the mean ±SD (n=3)

- **Evaluation of Post Compression Parameters**

Table: Evaluation of Floating Mucoadhesive Tablets of Rosiglitazone

Formulation Code	Thickness (mm) (mean±SD)	Average Weight(mg) (mean ±SD)	Hardness (Kg/cm ²) (mean ±SD)	Stability (%) (mean ±SD)	Content uniformity (%) (mean±SD)	Total Floating time (hrs) (mean±SD)	Floating Lag time (s) (mean±SD)
RF1	4.59±0.09	98.25±0.28	5.2±0.15	0.35±0.04	95.36±0.27	13±0.59	35.3±0.37
RF2	4.91±0.08	99.35±0.24	5.6±0.13	0.29±0.02	99.25±0.24	15.5±0.30	43.0±0.34
RF3	4.87±0.04	95.61±0.19	5.9±0.19	0.51±0.06	98.14±0.21	18±0.97	48.1±0.36
RF4	4.39±0.06	99.39±0.24	5.4±0.09	0.48±0.02	100.2±0.19	12.5±0.83	39.2±0.31

RF5	4.99±0.10	99.48±0.17	5.8±0.13	0.63±0.04	97.45±0.24	14±0.59	32.9±0.30
Note: Each worthspeaksto themean ±SD (n=3)							

• **In-vitro Release Studies**

'In-vitro drug release studies' were carried out in 0.1N HCl and the test reported that the release of rosiglitazone.

Table In-vitro dissolution data for formulations

Time(hr)	% Cumulative drug release		
	RF1	RF2	RF3
0	0	0	0
0.5	23.06	26.24	28.82
1	28.25	30.16	32.36
2	34.98	36.16	39.68
3	40.57	44.34	48.94

➤ **FTIR:**

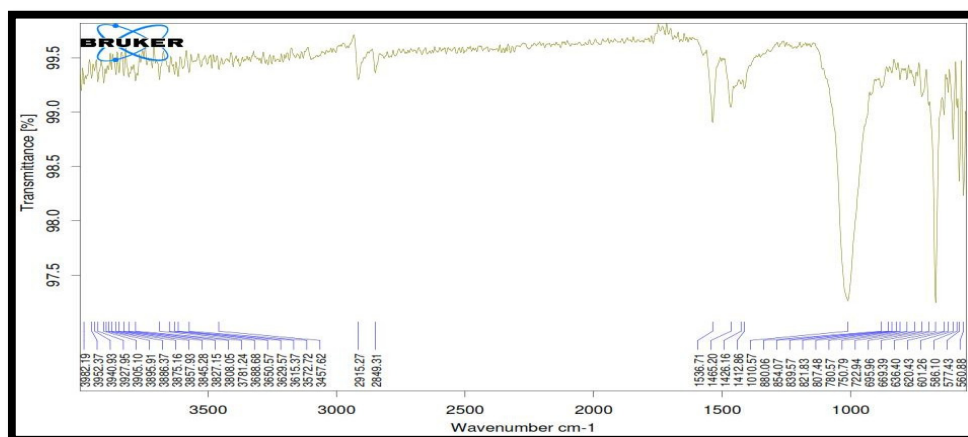


Figure: FT-IR of Rosiglitazone Pure Drug

The Fourier transform Infra-Red Spectroscopic Studie Infrared (IR) spectra were scanning series was lies in between 400 to 4000 cm^{-1} and the resolution was 1 cm^{-1} .

➤ **Differential Scanning Calorimetry(DSC)**

'Differential scanning calorimetry' (DSC) can be utilized to examine and foresee any physicochemical interaction between parts in detailing and along these lines can be applied to the choice of appropriate excipients.

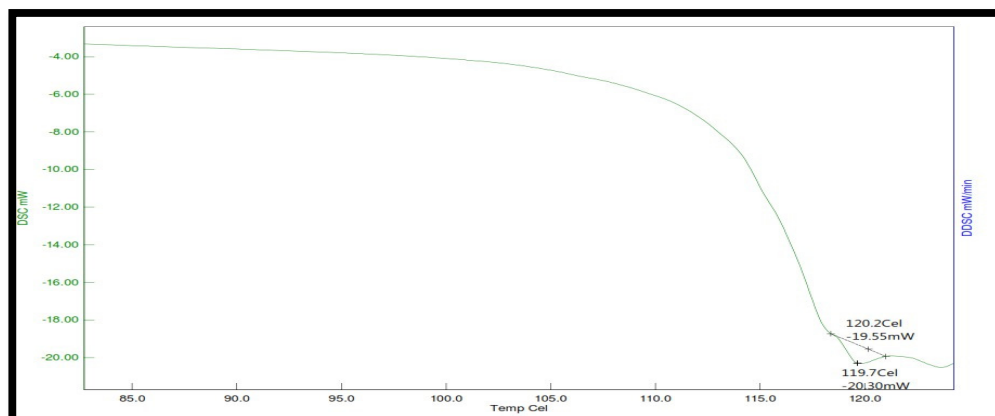


Figure: DSC of Rosiglitazone Pure Drug

• Conclusion

- From the obtained results, it can be concluded that the drugs can be easily formulated as GRDDS using different ratios of rate controlling polymers like chitosan, NaCMC, HPMC K200 and Carbopol 934.
- Chitosan is found to be promising polymer in controlling the rate and extent of drug release from the dosage form.
- Further work can be carried out to design more GRDDS.

• References

1. Siraj S, Khurshid MI. Current Trends in Gastroretentive Floating Bioadhesive Drug Delivery System. 25 April 2016.
2. Rouge N, Buri P, Doelker E, Drug absorption sites in the gastrointestinal tract and dosage forms for site specific. Delivery, Int. J. Pharm. 136 (1996) 117–139
3. Streube A, Siepmann J, Bodmeier R, Drug delivery to the upper small intestine window using gastro retentive technologies, Current Opinion in Pharmacology 2006, 6:501–508.
4. Prajapati VD, Raft forming system An upcoming approach of gastroretentive drug delivery system, Journal of Controlled Release 168 (2013) 151–165.
5. Bardonnnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastro retentive dosage forms: Overview and special case of Helicobacter pylori Journal of Controlled Release 111 (2006) 1 – 18.
6. Eswer G, Saritha M, Formulation and Evaluation of Atenolol Floating Tablets Using Different Polymers: Guar gum, Sodium Alginate, HPMC K100 and Carbopol 934, International Journal of Pharmaceutical & Biological Archives 2011; 2(4):1146-1151.
7. Someshwar K, Kalyani, Chithaluru K, Ramarao T, Kumar K, Formulation and evaluation of effervescent floating tablets of tizanidine hydrochloride, Acta Pharm. 61 (2011) 217–226.
8. Pattanayak D, Adepu R, Das S, Sura RS, A systemic review on Floating mucoadhesive drug delivery system, IAJPS 2018, 05 (04), 2970-2978.

9. Banker GS, Rhodes CT. Modern Pharmaceutics. Sustained and Controlled Release Delivery Systems. Marcel Dekker. 2002;4th :501-528.
10. Peddapalli H, Bakshi V, Boggula N, Formulation, in vitro and ex vivo characterization of mucoadhesive buccal tablets for antihypertensive drug, Asian J Pharm Clin Res, Vol 11, Issue 8, 2018, 402-411.
11. Hemnani M, Patel P, Patel G, Daslaniya D, Shah A, Matrix Tablets: A Tool of Controlled Drug Delivery, American Journal of Pharmatech Research. 1(4); 2249-3387:2011.
12. Sahel M, Al-Saidan, Krishnaiah YSR, Satyanarayana V. In-Vitro And In-Vivo Evaluation Of Guar gum Matrix Tablets For Oral Controlled Release Of Water-Soluble Diltiazem Hydrochloride. AAPS Pharm. Sci.Tech. 6(1) ; 31-36:2005.
13. Das S, Pattanayak D, Formulation and optimization of gastro retentive drug delivery system containing Glipizide, , International Journal of Pharmacy and Pharmaceutical Sciences, ; Vol 4, Issue 1, 2012, 203-205.
14. Alhamdany AT, Abbas AAK, formulation and In vitro evaluation of Amlodipine gastroretentive floating tablets using a combination of hydrophilic and hydrophobic polymers, Int J App Pharm, Vol 10, Issue 6, 2018, 126-134.
15. Nokhodchi A, Raja S, Patel P, Asare-Addo K, The Role Of Oral Controlled Release Matrix Tablets In Drug Delivery Systems, Bioimpacts. 2(4);175-187:2012.
16. Vyas SP, Khar RK. Controlled Drug Delivery Concepts and Advances. CBS Publishers, 2001;1st:1-53.
17. Siegel RA, Rathbone MJ, Departments of Pharmaceutics and Biomedical Engineering: Chapter 2: Overview of Controlled release mechanisms, Minneapolis. 2012:19-43.
18. Bramhanker DM, Jaiswal SB, Controlled Release Medications, Biopharmaceutics And Pharmacokinetics a Treatise. Vallabh Prakashan, 1995;2nd:335-375.
19. Peppas NA. Analysis of Fickian And Non-Fickian Drug Release From Polymers. Pharm.Acta.Helv. 60(4);110-111:1985.
20. Korsmeyer RW, Gurny R, Doelker E, Peppas NA, Mechanism of Solute Release From Porous Hydrophilic Polymers. Int. J. Pharm. 15;25-35:1983.