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Formulation and evaluation of floating tablet of rosiglitazone malate

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Abstract

Rosiglitazone Maleate is used for the management of type-2 diabetes. It is an absorption window limited drug, whose solubility decreases with increase in the pH and has a short half life of 3-4 h. Therefore the present investigation is concerned with the development of the floating matrix tablets, which after oral administration were designed to prolong the gastric residence time and thus to increase the bioavailability of the drug and its half life. Rosiglitazone Maleate showed maximum absorption at wavelength 222 nm in 0.1N HCl. Drug-polymer compatibility studies by DSC gave conformation about their purity and showed no interaction between drug and selected polymers. Various formulations were developed by using release rate controlling and gel forming polymers like HPMC, NaCMC and Carbopol-934 in single and combinations by direct compression method with the incorporation of sodium bicarbonate as gas generating agent. All the formulations had floating lag time below 4 minutes and constantly floated on dissolution medium for more than 12 h. Swelling studies indicated significant water uptake and contributed in drug release. DCP showed maximum drug release retardation compared to lactose and MCC. From among all the developed formulations, as F7, F14 and F21 prolonged the drug release for longer period of time, they were nominated as best formulations. The best formulations followed power law kinetics while the drug release mechanism was found to be anomalous type, diffusion through the honeycomb network and polymer relaxation. The best formulations were found to be stable during stability studies for two months. Thus, best formulations satisfied physico-chemical parameters, floating time, swelling index and in vitro drug release profile requirements for a floating drug delivery system.

Key-Words: Rosiglitazone Maleate; Floating Drug Delivery System; Floating Matrix tablet; Stability Study

Introduction

The millennium has dawned. Development of newer drugs and medicines will be the goal of scientists across the world. In order to achieve satisfying results, a drug has to be properly formulated in proper dosage form. It is an established fact that the conventional immediate release drug delivery systems when taken frequently in a day can maintain drug concentration levels in therapeutically effective range. However, this results in significant fluctuations in plasma drug levels. Recently, several technical advancements have led to the development of various Novel Drug Delivery Systems (NDDS) that could revolutionize method of drug delivery and hence could provide definite therapeutic benefits.[1]

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Till date, man has found remedies for almost all diseases; but still research is going on in order to improve the existing therapy. To bring a new drug molecule, it involves a lot more than investment of time and money. In the pre GATT era, If the patents of drug molecules/formulations were expiring, the new way of patenting the drug is to use "Novel Drug Delivery Systems" i.e. NDDS with improved bio-availability. To formulate a drug or to re-formulate it in a form of NDDS is not a herculean task if one goes methodically and skillfully. This is where the formulation development studies play an important role.

An oral drug delivery system providing a uniform drug delivery can only partly satisfy therapeutic and biopharmaceutical needs, as it doesn't take into account the site specific absorption rates within the gastrointestinal tract, therefore there is need for developing delivery system that release the drug at the right time, at the specific site and with the desired rate.

The most important objective for the development of controlled release dosage forms systems is to furnish an extended duration of action and thus assure greater patient compliance. Pharmacokinetically, it is often desirable to administer a single dose of medication, which release the active ingredient over an extended period of time rather than to administer a number of single doses at regular intervals.[2-3]

Application of FDDS[4-6]

- Recent study indicated that the administration of Diltiazem floating tablets twice a day might be more effective compared to normal tablets in controlling the blood pressure of hypertensive patients.
- Modapar® HBS containing L-DOPA and Benserazide, here the drug was absorbed over a period of 6-8 h and maintained substantial plasma concentration for Parkinsonian patients. Cytotech®- containing Misoprostol, a synthetic prostaglandin–EL analogue, for prevention of gastric ulcer caused by non-steroidal anti-inflammatory drugs (NSAIDS).
- Site specific drug delivery: These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., Riboflavin and Furosemide.
- Absorption Enhancement: Ichikawa et all developed a multiparticulate system that consisted of floating pills of a drug (p- amino benzoic acid) having a limited absorption site in the gastrointestinal tract. It was found to have 1.61 times greater AUC than the control pills.
- FDDS also serves as an excellent drug delivery system for the eradication of *H. pylori*, which causes chronic gastritis and peptic ulcers.
- Developing HBS dosage form for Tacrin provide better delivery systems and reduced its GI side effects.
- Treatment of gastric and duodenal ulcer.

Material and methods

Dose selection

The 8 mg daily dose of Rosiglitazone maleate has been shown to be safe and effective in clinical studies as monotherapy. Therefore 8 mg dose was selected for the designing of floating drug delivery system in the present study. 10.6 mg Rosiglitazone maleate equivalent to 8 mg rosiglitazone.[7]

Drug polymer compatibility studies

Drug polymer compatibility studies were carried out using DSC. The DSC analysis was carried out at a heating range of 54 °C to 300 °C at a heating rate of 10 °C/min. The study was carried out on individual pure drug and its physical mixture with the selected polymers under study.[8]

Identification of drug

Development of calibration curve

Rosiglitazone Maleate equivalent to 10 mg of Rosiglitazone was weighed accurately and added to 10 ml volumetric flask. It was dissolved in 1ml of ethanol and volume was made with 0.1 N HCl to get a stock solution. From the stock solution 0.4, 0.8, 1.2, 1.6, 2.0 ml were pipette out to get 4, 8, 12, 16 and 20 ppm solutions. Absorbance of each of these was recorded at 222 nm.

UV Spectrum analysis of rosiglitazone maleate

The solution was scanned in the range of 200 to 400 nm to fix the maximum wave length and UV spectrum was obtained.

Formulation development of floating tablets

Various formulations of floating tablets were developed for Rosiglitazone maleate using various polymers like HPMC, NaCMC, Carbopol-934; filler like lactose, MCC and DCP. Sodium bicarbonate was selected as gas generating agent. Magnesium stearate was used as lubricant.

Method of preparation of floating tablets

Rosiglitazone maleate, selected polymers, sodium bicarbonate and lactose were taken in required quantities and passed through 60 mesh separately. In dry state, the drug with other ingredients was mixed for the period of 10 min in mortar to get uniform mixture power. The mixture was blended with Magnesium stearate for 2-3 min. to improve flow property. The powder was compressed into tablets using a Rotary tablet press.

Evaluation

Tablet thickness

Thickness of tablets was important for uniformity of tablet size. Thickness was measured using Vernier Calipers on 3 randomly selected samples.[9]

Tablet hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester. [9]

Friability

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4

min., the tablets were weighed and the percentage loss in tablet weight was determined. [9]

Weight variation

Twenty tablets were weighed individually and the average weight was determined. The % deviation was calculated and checked for weight variation as per IP. [10]

Uniformity of content

Content of active ingredient in tablets was taken at random, was determined. 10 tablets were weighed and average weight is calculated. All tablets were crushed and powder equivalent to 8 mg was dissolved in 250 ml 0.1 N HCl and shaken for 20 min. solution was filtered and after suitable dilution using 0.1 N HCL, absorbance was measured spectrophotometrically at 222 nm against reagent blank. Amount of drug present in one tablet was calculated. [10]

Floating lag time

The lag time was carried out in beaker containing 100 ml of 0.1 N HCl as a testing medium maintained at 37 ˚C. The time required for the tablet to rise to the surface and float was determined as floating lag time. [06]

Floating time

Floating time was the time, during which the tablet floats in 0.1 N HCL dissolution medium (including floating lag time). [06]

Swelling characteristics

The swelling properties of matrix tablet containing drug were determined by placing the tablet matrices in the USP Dissolution Testing Apparatus II, in 900 ml of 0.1 N HCl at 37 ± 0.5 ˚C, rotated at 50 rpm. The tablets were removed periodically from dissolution medium, blotted to remove excess water and weighed. Swelling characteristics were expressed in terms of percentage water uptake (WU %) according to the equation. [11]

Dissolution studies

The release rate of Rosiglitazone Maleate from floating tablets was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5 ˚C and 50 rpm. Aliquot volume was withdrawn from the dissolution apparatus hourly for 12 h, and the samples were replaced with fresh dissolution medium. After filtration and suitable dilution the amount of drug release was determined from the calibration curve. [06, 13]

Details of Dissolution Test

Apparatus	: USP Type II
Volume of medium	: 900 ml
Temperature	: 37 ˚C
Paddle Speed	: 50 rpm
Dissolution medium used	: 0.1 N HCl
Aliquot taken at each time interval	: 10 ml

Analysis of release mechanism

The release data were treated by the Ritger and Peppas equation also called as Power law. The equation was treated logarithmically to determine the value of release exponent, *n*; the value of *n* is indicative of mechanism of drug release. [13]

$$Mt/M_\infty = kt^n$$

Where *Mt/M* is the fraction of drug released at time *t*,
k – Kinetic constant of the tablet.
n – Release exponent.

The *n* value of 1 corresponds to zero-order release kinetics, 0.5<n<1 indicates a non-Fickian release model or anomalous transport and n=0.5 indicates Fickian diffusion .From the plot of log (*Mt/M*) versus log *t*; the kinetic parameters *n* and *k* were calculated.

Stability studies of the standardized formulations

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines Q1C. [14]

The stability studies were carried out on the most satisfactory formulations as per ICH guidelines Q1C. The most satisfactory formulation sealed in aluminum packaging and kept in humidity chamber maintained at 35 ± 2 °C / 60 ± 5 %RH and 40 ± 2 °C / 75 ± 5 %RH for 2 months. At the end of studies, samples were analyzed for the drug content, in vitro dissolution, floating behavior and other physicochemical parameters.

An attempt has been made to formulate floating tablet of Rosiglitazone Maleate as it has narrow absorption window in GIT due to its poor solubility at alkaline pH. The floating tablets were evaluated for various physical parameters like thickness, weight variation, hardness, % drug content, floating lag time, floating time, swelling studies, *in vitro* drug release and stability studies.

Results and discussion

Rosiglitazone is one of the drugs, which is used for the management of type-2 diabetes. It is an absorption window limited drug, whose solubility decreases with increase in the pH and has a short half life of 3-4 h.

One of the most feasible drug delivery system for such a drug is controlled release gastro-retentive dosage form. Floating drug delivery system is considerably easy and logical approach in the development of gastro-retentive dosage forms.

The real requirement in the development of gastro-retentive controlled release dosage form is not only to prolong the delivery of drugs for longer duration of time but also to prolong the presence of dosage forms in the stomach.

The present investigation is concerned with the development of the floating matrix tablets, which after oral administration were designed to prolong the gastric residence time, thus to increase the bioavailability of the drug and its half life.

At the outset, method for the estimation for the drug was developed. Rosiglitazone Maleate showed maximum absorption at wavelength 222 nm in 0.1N HCl. Standard calibration curve obeyed Beer's law at given concentration range of 4 µg/ml to 20 µg /ml and when subjected to regression analysis, the value of regression co-efficient was found to be 0.9917, which showed linear relationship between concentration and absorbance.

The thermogram of Rosiglitazone Maleate displayed a single sharp endothermic peak at 124.702 °C, which corresponds to the melting point of the pure drug. The Melting Endotherms of physical mixture of drug with selected polymers gave peak which corresponded to the melting point of the pure drug which conform the compatibility between drug and selected polymers.

Various formulations of floating tablets were developed for Rosiglitazone maleate using various polymers like HPMC, NaCMC, Carbopol-934; various fillers like lactose, MCC and DCP; Sodium bicarbonate was used as gas generating agent. Magnesium stearate was used as lubricant. The various developed formulations of floating tablets were prepared by direct compression method using 7 mm flat punches to an average weight of 150 mg.

Thickness of the formulations F1 to F21 varied from 2.28 ± 0.015 mm to 2.76± 0.015 mm. Hardness of the formulations F1 to F21 varied from 5.16 ± 0.28 to 6.33 ± 0.57 kg/cm^2. Friability of the formulations F1 to F21 varied from 0.12 to 0.58 %. The average weight of 20 tablets varied from 147.66 ± 3.79 mg to 151.50 ± 3.20 mg, which comply the official requirement of IP. Drug content of the formulations F1 to F21 varied from 96.06 ± 1.57% to 102.86 ± 2.71%, which comply as per pharmacopoeial standard.

Buoyancy lag time of all the developed formulations F1 to F21 varied from 3.00 ± 1.0 seconds to 259.66 ± 6.50 seconds. As the concentration of high molecular weight of polymer increase and hydrophilic grades of polymers decrease floating lag time decrease.

Floating time was found to depend on types of polymers & their concentration, swelling property, degree of gelling and their gel strength. All the developed matrix tablets showed a floating time of 12 h.

In the present study, sodium bicarbonate served two purposes like, along with making the tablet to float, it also acted as buffering agent as the solubility of Rosiglitazone maleate decrease as increase in the pH in the GIT.

Floating time was found to be depending on types of polymer & its concentration, swelling property, degree of gelling and gel strength. All the developed matrix tablets showed the floating time up to 12 h.

The percentage water uptake of the formulations F1 to F21 varied from 40.32 % to 128.64 %. Concentration and viscosity of polymer showed directly proportional relationship with swelling characteristics of tablets. Anionic polymers had possible ionic interaction with the nonionic polymers, which resulted in favorable increase in the water uptake capacity and gel viscosity, leading to a better control over the release of Rosiglitazone Maleate.

The release of Rosiglitazone Maleate from floating tablets varied according to types and proportion of matrix forming polymers. The use of mixture of polymers represents a potential way of achieving a variety of release properties.

The duration of drug release was slower with formulation F4 which was about only 79.46±0.94 % in 12th h from among the formulations F1 to F5. The duration of drug release was prolonged with the formulation F8 which was about only 75.46 ± 1.17 % in 12th h from among the formulations F8 to F12. The formulation F16 released the drug with slower rate of 94.84 ± 0.89 % in 12th h among formulations F15 to F19. The higher viscosity polymer had been seen to inhibit the initial burst effect of Rosiglitazone from the FDDS.

The formulations F4, F8 and F16 prolonged the release over longer period of time. Therefore they were selected to study the effect of diluents on drug release profile. When DCP was used as diluent in the formulations F7, F14 and F21, the drug release was 76.21±0.93%, 70.48±0.94% and 87.92±0.65% respectively at 12th h of dissolution studies. It was found from results that DCP prolonged drug release compare to Lactose and MCC.

From among all the developed formulations, since formulations F7, F14 and F21 prolonged the drug release for longer period of time, of beyond 12th h, they were selected as the most satisfactory formulations.

The release data of the most satisfactory formulation were treated by Ritger and Peppas equation. The correlation co-efficient R^2 value of most satisfactory formulations F7, F14 and F21 were found to be 0.9843, 0.9825 and 0.9625 respectively, which showed a linear relationship with R^2 value close to 1.

The release exponent *n* value of standardized formulations F7, F14 and F21 were found to be 0.7288, 0.7104 and 0.7462 which lied between $0.5 < n < 1$,

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indicating diffusion controlled release as well as swelling controlled release.

The stability studies were carried out on the most satisfactory formulations as per ICH guidelines Q1C. At various time intervals of 30 days and 60 days end, samples were evaluated. There were no major changes in the various physico-chemical parameters evaluated like hardness, drug content and floating properties at the various sampling points. There was no statistically significant difference between the initial values and the results obtained during stability studies. The floating behavior of the gastro-retentive drug delivery system could successfully be combined with accurate control of the drug release patterns.

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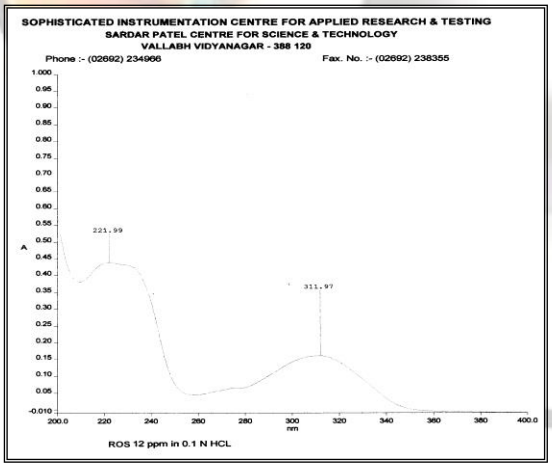
Fig. 4: UV Spectrum of rosiglitazone maleate in pH 1.2

Fig. 5: Standard calibration curve of rosiglitazone maleate



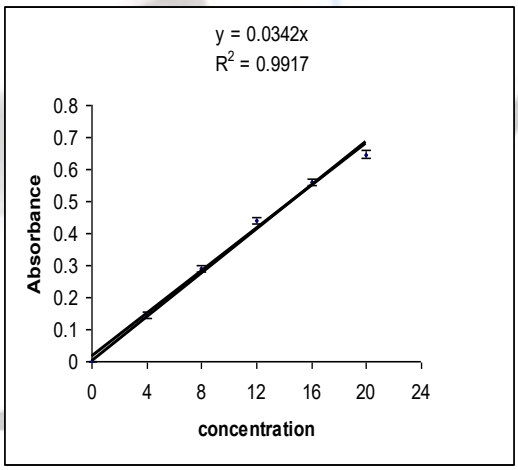


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Table 3: Concentration and absorbance obtained for standard plot of rosiglitazone maleate in 0.1N HCl buffer

Concentration (µg/ml)	Absorbance* (At 222 nm)	Variance*
0	0	0.0
4	0.14387±0.009277	0.000086
8	0.28773±0.009816	0.000096
12	0.43827±0.009601	0.000092
16	0.56108±0.00954	0.000091
20	0.6474±0.011534	0.000133

*** Average of 3 readings**

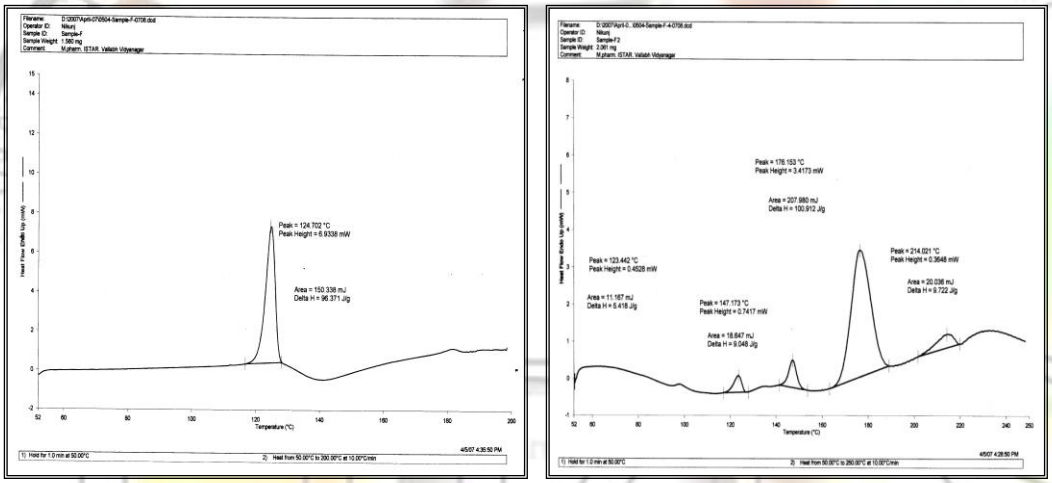

Fig. 6: DSC of pure rosiglitazone maleate

Fig. 7: DSC of physical mixture of rosiglitazone maleate with HPMC and CP-934

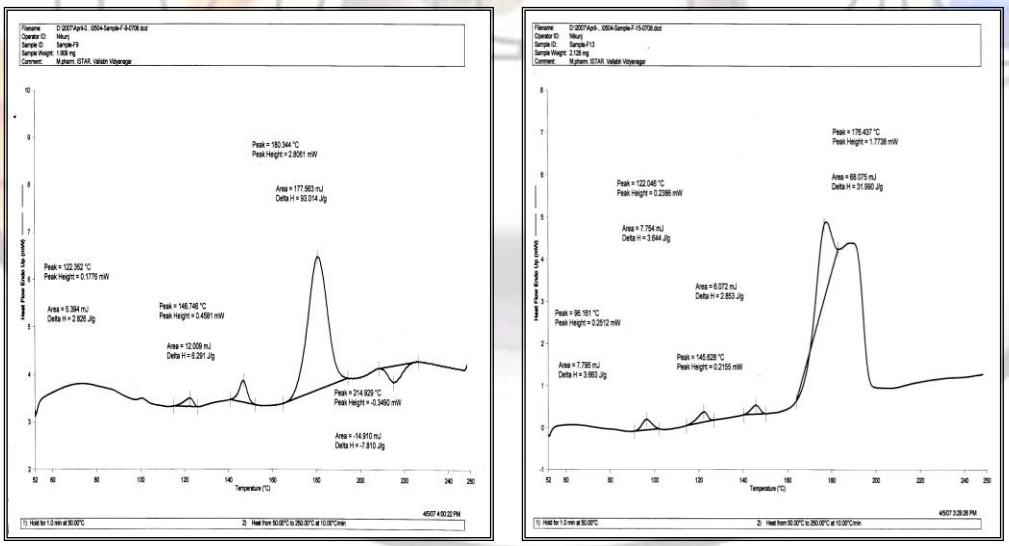

Fig. 8: DSC of physical mixture of rosiglitazone maleate with CP-934 and NaCMC

Fig. 9: DSC of physical mixture of rosiglitazone maleate with NaCMC and HPMC

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Table 4: Formulas of floating matrix tablets developed

Ingredients (Mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21
HPMC K4M	100	75	50	25	15	25	25	-	-	-	-	-	-	-	-	25	50	75	85	25	25
Carbopol 934	-	25	50	75	85	75	75	100	75	50	25	15	100	100	-	-	-	-	-	-	-
Na CMC	-	-	-	-	-	-	-	-	25	50	75	85	-	-	100	75	50	25	15	75	75
Lactose	18	18	18	18	18	-	-	18	18	18	18	18	-	-	18	18	18	18	18	-	-
MCC	-	-	-	-	-	18	-	-	-	-	-	-	18	-	-	-	-	-	-	18	-
DCP	-	-	-	-	-	-	18	-	-	-	-	-	-	18	-	-	-	-	-	-	18
$NaHCO_3$	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Mg-Stearate	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
Total weight	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150

- All the formulations contained 10.6 mg of Rosiglitazone Maleate equivalent to 8 mg of Rosiglitazone

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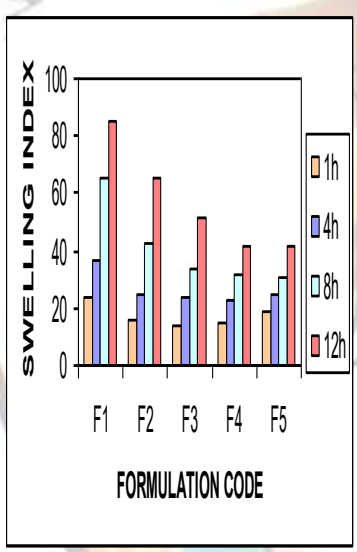
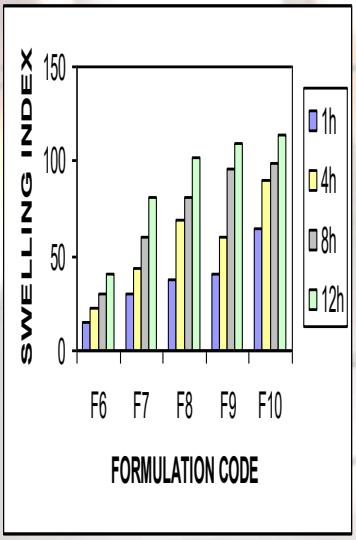
Table 5: Swelling characteristics

Formulations	Time (h)			
	1	4	8	12
F1 (%)	23.8	36.15	65.32	85.32
F2 (%)	15.4	24.45	42.46	65.23
F3 (%)	14.34	14.34	33.3	51.32
F4 (%)	15.32	23.06	31.66	41.16
F5 (%)	18.78	25.16	30.7	41.54
F8 (%)	15.6	22.02	30.44	40.32
F9 (%)	29.41	43.25	60.71	81.35
F10 (%)	37.158	69.25	80.26	101.32
F11 (%)	41.23	60.54	96.58	110.25
F12 (%)	64.36	90.26	108.29	114.65
F15 (%)	40.14	56.65	74.64	116.34
F16 (%)	53.45	74.54	104.64	122.65
F17 (%)	60.71	95.36	114.62	130.65
F18 (%)	46.65	62.36	102.64	118.64
F19 (%)	26.39	42.09	68.64	92.69





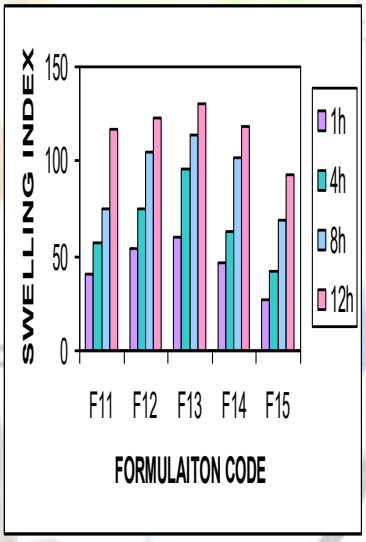


Fig. 10: Swelling index of HPMC and Carbopol-934 based tablets
Fig. 11: Swelling index of NaCMC and Carbopol-934 based tablets
Fig. 12: Swelling index of NaCMC and HPMC based tablets

Table- 7: Drug release profiles of various formulations of developed floating tablets

TIME (h)	F1 %	F2 %	F3 %	F4 %	F5 %	F8 %	F9 %	F10 %	F11 %	F12 %	F15 %	F16 %	F17 %	F18 %	F19 %
1	21.35 ±1.12	17.67 ±0.60	15.85 ±0.54	14.75 ±0.5	16.41 ±1.11	15.25 ±0.98	18.58 ±0.56	15.47 ±0.69	19.34 ±0.96	20.64 ±1.29	17.41 ±1.13	18.8 ±0.83	20.68 ±0.93	26.39 ±1.09	23.35 ±1.07
2	27.37 ±1.00	22.38 ±1.04	19.62 ±1.07	18.6 ±0.73	19.46 ±1.05	18.28 ±1.06	25.88 ±0.42	19.38 ±0.69	25.61 ±1.04	26.52 ±1.1	22.39 ±1.16	24.6 ±0.74	26.81 ±0.43	34.58 ±0.95	29.35 ±0.85
3	33.45 ±1.25	28.60 ±0.99	25.74 ±1.14	23.35 ±1.11	23.20 ±0.89	23.15 ±0.95	29.9 ±0.75	26.43 ±0.72	29.62 ±0.92	31.2 ±1.17	29.40 ±1.06	30.25 ±1.11	31.91 ±0.70	39.34 ±1.07	35.57 ±1.26
4	41.3 ±0.65	34.83 ±0.84	30.49 ±1.14	27.45 ±0.90	26.7 ±1.12	28.47 ±0.89	35.03 ±0.99	30.40 ±0.90	36.24 ±1.03	39.28 ±0.95	33.34 ±0.93	36.70 ±0.94	37.78 ±0.58	47.46 ±1.88	46.19 ±1.66
5	48.74 ±2.27	40.42 ±1.04	38.53 ±1.19	35.31 ±1.11	32.58 ±1.22	32.39 ±099	38.84 ±0.52	37.39 ±0.88	43.28 ±1.02	45.58 ±1.33	40.44 ±1.08	42.65 ±1.31	43.53 ±0.62	58.44 ±1.18	54.41 ±1.12
6	57.13 ±1.89	48.50 ±0.89	47.43 ±0.95	41.27 ±1.04	37.34 ±0.97	36.32 ±0.9	46.75 ±0.34	45.72 ±1.17	48.52 ±1.25	51.75 ±1.09	45.71 ±0.65	51.47 ±1.11	51.78 ±0.77	65.20 ±0.91	62.66 ±1.37
7	68.35 ±0.83	57.20 ±0.99	53.41 ±0.98	49.97 ±1.65	45.47 ±0.68	42.56 ±1.26	52.17 ±0.52	52.47 ±1.21	52.72 ±0.97	59.43 ±0.94	52.36 ±0.8	58.79 ±1.70	58.93 ±0.90	74.25 ±0.96	71..5 ±1.26

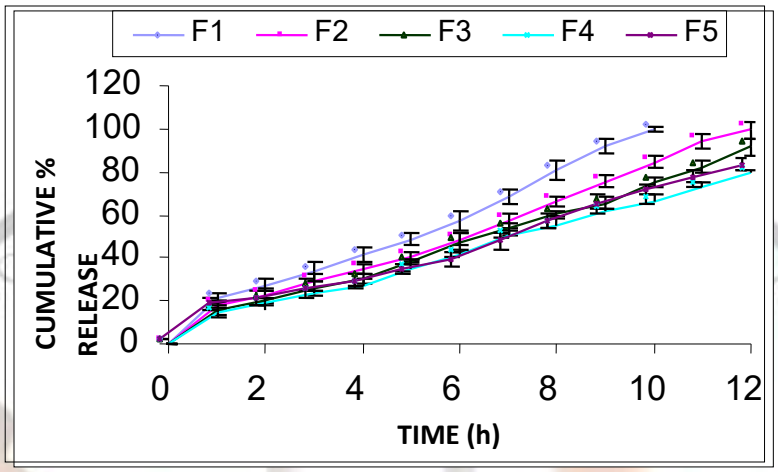


Fig. 13: Drug release profile of HPMC and Carbopol-934 based tablets

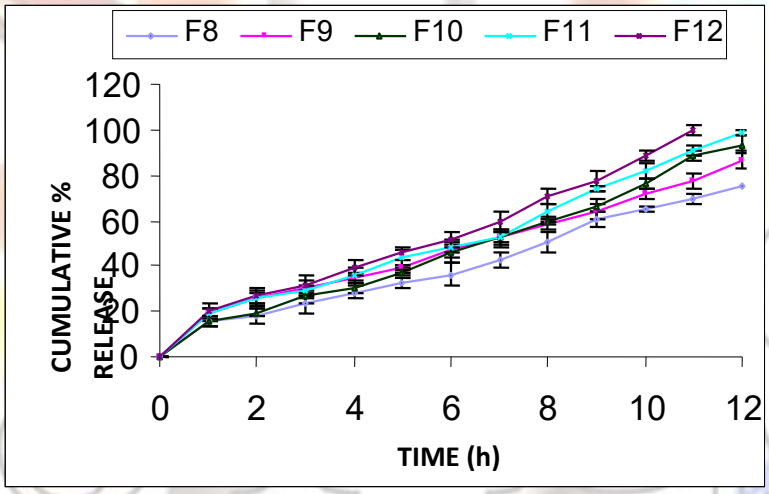


Fig. 14: Drug release profile of NaCMC and Carbopol-934 based tablets

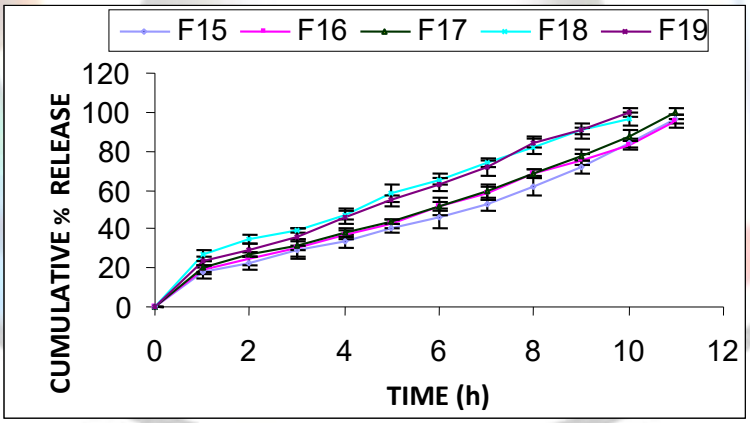


Fig. 15: Drug release profile of NaCMC and HPMC based tablets

Table 9: Effect of Diluents on Release Profiles of the Standardized formulations

Time (h)	Effect of diluents on % drug release profile*								
	F4 %	F6 %	F7 %	F8 %	F13 %	F14 %	F16 %	F20 %	F21 %
1	14.75 ±0.5	15.47 ±0.69	13.45 ±0.56	15.25 ±0.98	18.58 ±0.56	13.12 ±0.45	18.8 ±0.83	17.26 ±1.25	15.78 ±0.79
2	18.6 ±0.73	19.38 ±0.69	17.45 ±0.98	18.28 ±1.06	25.88 ±0.42	17.69 ±0.46	24.6 ±0.74	23.35 ±1.07	20.68 ±0.93
3	23.35 ±1.11	26.43 ±0.72	22.81 ±0.64	23.15 ±0.95	29.9 ±0.75	22.36 ±1.45	30.25 ±1.11	29.35 ±0.85	26.81 ±0.43
4	27.45 ±0.90	30.40 ±0.90	26.74 ±0.95	28.47 ±0.89	35.03 ±0.09	29.36 ±0.45	36.70 ±0.94	35.57 ±1.26	31.91 ±0.70
5	35.31 ±1.11	37.39 ±0.88	31.26 ±0.87	32.39 ±099	38.84 ±0.52	34.51 ±1.26	42.65 ±1.31	40.15 ±0.89	37.78 ±0.58
6	41.27 ±1.04	45.72 ±1.17	35.41 ±0.74	36.32 ±0.9	46.75 ±0.34	38.02 ±0.89	51.47 ±1.11	46.19 ±1.66	43.53 ±0.62
7	49.97 ±0.35	52.47 ±1.21	40.89 ±1.20	42.56 ±1.26	52.17 ±0.52	42.36 ±0.89	58.79 ±1.70	54.41 ±1.12	51.78 ±0.77
8	55.33 ±1.14	59.41 ±0.75	51.26 ±0.41	50.35 ±1.04	58.81 ±0.57	49.36 ±1.82	68.34 ±0.91	62.66 ±1.37	58.93 ±0.90
9	61.40 ±1.12	66.56 ±1.26	58.36 ±0.46	60.01 ±0.28	63.87 ±0.23	55.12 ±0.47	75.64 ±1.39	74.5 ±1.26	68.74 ±0.63
10	66.42 ±1.19	76.55 ±0.98	65.41 ±0.65	64.63 ±0.45	71.69 ±0.39	59.31 ±1.68	83.48 ±1.03	86.45 ±0.88	77.78 ±1.03
11	73.27 ±1.02	88.35 ±0.71	71.26 ±0.45	69.96 ±1.31	77.46 ±0.59	65.12 ±1.56	94.84 ±0.5	99.64 ±0.57	87.92 ±0.65
12	79.48 ±0.94	93.52 ±0.79	76.21 ±0.93	75.46 ±1.17	86.89 ±0.19	70.48 ±0.94	---	---	---

*** Average of 3 readings**

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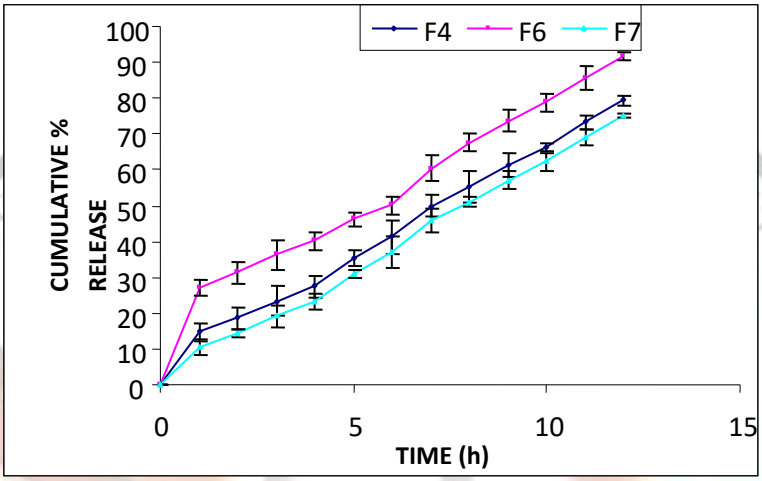

Fig. 16: Effect of diluents on dissolution profiles of formulations F4, F6 & F7

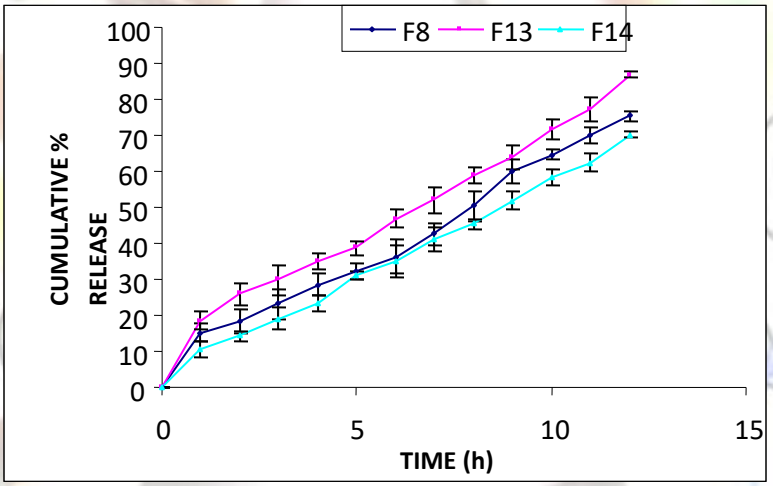

Fig. 17: Effect of diluents on dissolution profiles of formulations F8, F13 & F14

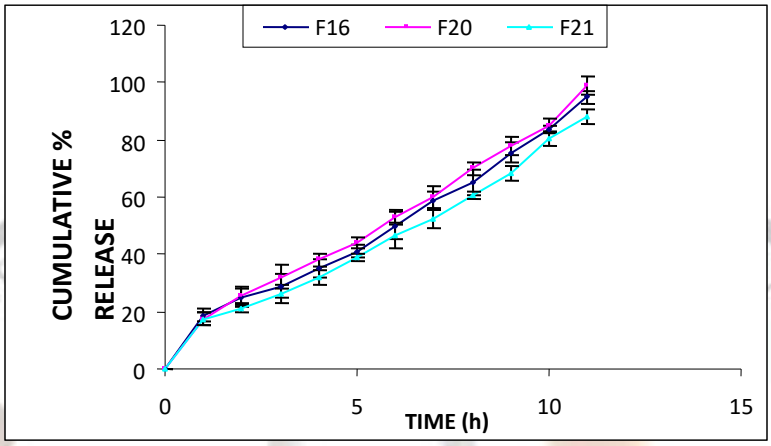

Fig. 18: Effect of diluents on dissolution profiles of formulations F16, F20 & F21

Table 8: Release kinetics parameters of rosiglitazone maleate from the most satisfactory formulations of floating tablets

Formulations	Release exponent (n)	Kinetic Constant (k)	Correlation Coefficient (R^2)
F7	0.7288	1.075	0.9843
F14	0.7104	1.0486	0.9825
F21	0.7462	1.0946	0.9625

Table 10: Drug release profiles of the most satisfactory formulations during stability studies

Time (h)	After 30 Days*						After 60 Days*					
	A			B			C			D		
	F7 %	F14 %	F21 %	F7 %	F14 %	F21 %	F7 %	F14 %	F21 %	F7 %	F14 %	F21 %
1	10.27 ±0.53	12.96 ±0.93	15.64 ±0.63	13.63 ±0.75	12.95 ±0.59	18.36 ±0.65	20.36 ±0.53	16.95 ±0.54	20.65 ±0.54	12.34 ±0.45	13.04 ±0.61	19.69 ±0.65
2	17.15 ±0.64	16.54 ±0.54	22.36 ±0.65	18.21 ±1.25	17.43 ±0.81	23.36 ±1.04	26.31 ±0.65	21.48 ±1.04	26.82 ±0.43	18.51 ±1.68	19.85 ±1.04	25.36 ±0.43
3	22.36 ±0.91	21.36 ±0.64	28.36 ±0.65	25.31 ±2.49	22.71 ±0.84	29.48 ±0.45	30.42 ±0.74	26.15 ±2.45	31.84 ±0.51	23.64 ±0.99	24.02 ±0.92	30.36 ±0.64
4	27.15 ±0.65	25.15 ±1.08	34.31 ±0.64	31.14 ±0.85	26.94 ±1.85	35.83 ±0.93	37.24 ±1.04	31.95 ±0.36	37.89 ±0.65	29.36 ±0.65	29.26 ±1.09	36.84 ±0.65
5	32.78 ±1.03	30.15 ±1.05	39.36 ±2.95	38.15 ±1.82	31.74 ±0.67	41.36 ±1.65	42.46 ±0.69	35.15 ±0.96	43.65 ±0.94	36.64 ±0.96	35.35 ±012	42.45 ±0.65
6	38.26 ±0.65	36.72 ±1.65	46.16 ±0.65	43.29 ±0.62	35.19 ±1.43	49.36 ±0.65	49.36 ±1.06	41.62 ±1.05	49.95 ±0.65	41.78 ±0.94	39.36 ±1.06	49.65 ±0.56
7	44.36 ±0.65	41.94 ±0.64	52.36 ±0.65	49.36 ±0.71	42.94 ±0.49	58.31 ±0.65	53.36 ±0.65	45.79 ±0.65	55.65 ±0.69	46.65 ±0.56	44.36 ±0.15	55.26 ±0.65
8	51.12 ±0.48	48.31 ±1.09	58.63 ±0.36	56.36 ±0.94	49.55 ±1.64	65.36 ±0.63	59.61 ±1.02	49.45 ±1.06	62.64 ±0.64	52.36 ±0.56	51.36 ±1.66	62.36 ±0.64
9	57.19 ±2.26	53.98 ±1.06	65.23 ±1.00	62.15 ±2.51	53.15 ±1.69	73.36 ±0.69	65.94 ±1.02	56.26 ±1.06	70.65 ±1.06	58.36 ±0.65	55.36 ±1.06	71.36 ±0.33
10	64.79 ±1.10	59.71 ±1.01	72.36 ±0.59	67.35 ±1.49	58.61 ±1.86	81.36 ±1.25	70.49 ±1.48	61.65 ±0.36	77.65 ±0.65	63.36 ±0.36	59.64 ±0.36	79.69 ±0.23

11	69.18 ±230	65.34 ±0.96	82.65 ±0.95	73.92 ±1.57	64.94 ±1.64	89.36 ±1.15	74.36 ±1.01	67.46 ±0.36	85.64 ±0.15	68.36 ±1.14	65.36 ±0.36	87.21 ±0.15
12	75.31 ±0.76	73.17 ±0.65		78.17 ±0.64	69.76 ±0.83		79.65 ±0.65	72.69 ±0.65		73.36 ±0.98	71.98 ±0.95	

A, C = 30 ± 2 °C / 65 ± 5 % RH
B, D = 40 ± 2 °C / 75 ± 5 % RH
*** Average of 3 readings**

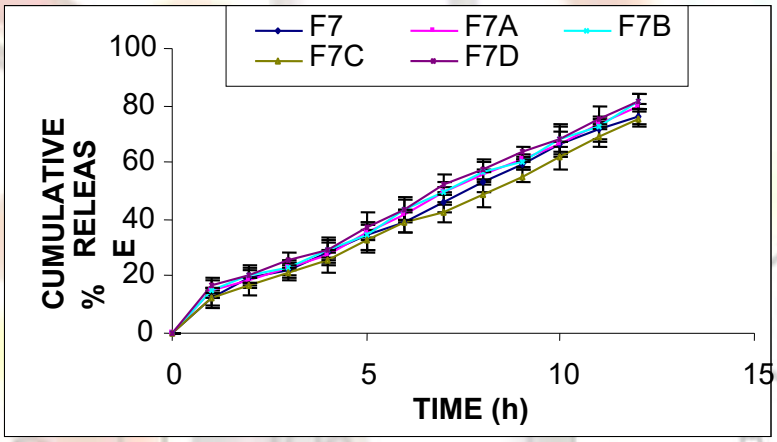

Fig. 19: Drug release profile of F7 during stability studies

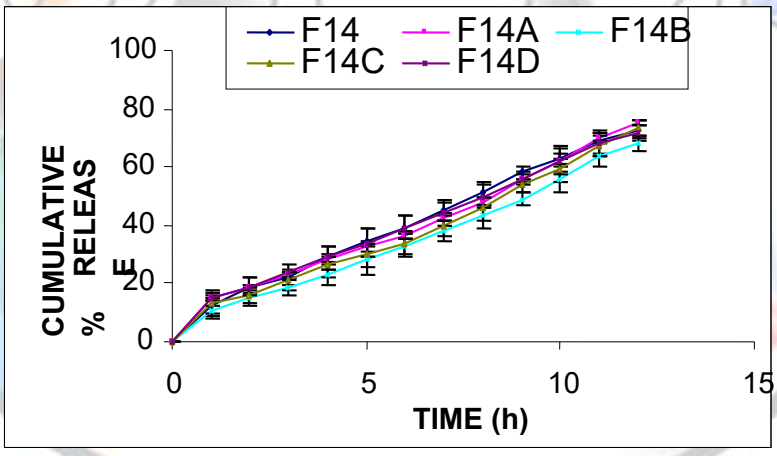

Fig. 20: Drug release profile of F14 during stability studies

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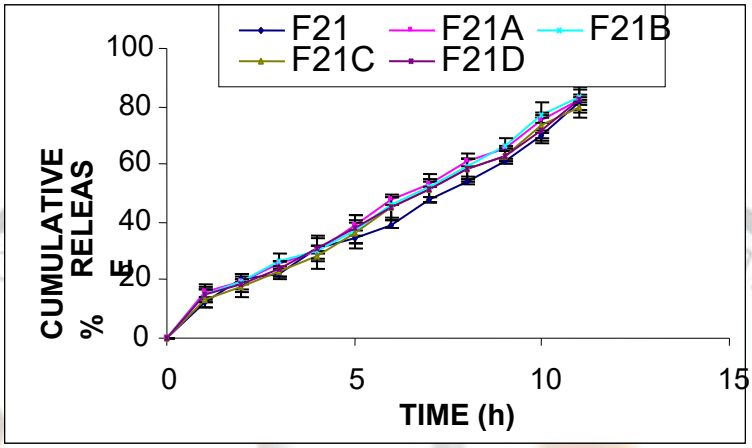

Fig. 21: Drug release profile of F21 during stability studies

Table 11: Physico-chemical characterization of most satisfactory formulations during stability studies

		F7	F14	F21
Floating Lag Time* (sec)	F7	17.66 ±2.51	25.8 ±12.3	21.7 ±6	19.2 ± 17	27.5 ± 9
	F14	3.00 ±1.0	6.23 ±17.6	4.82 ±13.3	7.67 ±4.3	5.26 ±3.7
	F21	238 ±10.69	225 ±3.24	244 ±15.6	231 ±4.62	248 ±3.67
% Drug content *	F7	99.19 ±2.23	99.65 ±1.86	98.63 ±3.45	99.79 ±2.85	98.31 ±2.65
	F14	98.48 ±3.45	98.93 ±2.46	98.78 ±2.46	99.94 ±1.62	99.31 ±2.32
	F21	102.71 ±2.79	99.68 ± 3.21	98.23 ±1.74	99.88 ±3.45	98.39 ±3.25

* Average of 3 readings

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Time (Days)		Hardness* (Kg/cm²) F7	Hardness* (Kg/cm²) F14	Hardness* (Kg/cm²) F21
0		6.33 ±0.33	5.16 ±0.16	5.66 ±0.28
30	At 30±2°C 65±5%RH	6.23 ±0.42	5.28 ±0.25	5.86 ±0.32
	At 40±2°C 75±5%RH	6.45 ±0.64	5.32 ±0.12	5.63 ±0.43
60	At 30±2°C 65±5%RH	6.53 ±0.34	5.23 ±0.36	5.81 ±0.17
	At 40±2°C 75±5%RH	6.35 ±0.45	5.35 ±0.26	5.75 ±0.24