IJSRM
INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY
An Official Publication of Human Journals

Human Journals
Research Article
March 2020 Vol.:15, Issue:1

Preparation and Evaluation of Non-Effervescent Tablets

IJSRM
INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY
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Submission: 22 February 2020
Accepted: 29 February 2020
Published: 30 March 2020

Keywords: Pioglitazone, Direct Compression, Non-Effervescent Tablets

ABSTRACT

The Non-effervescent Floating matrix tablets were prepared by direct compression method. All the ingredients were blended to get a homogenous mixture. Accurel® MP1000 as low-density polypropylene foam powder, Aloe vera gel powder as release retardant, Carrageenan gum as swellable polymer, lactose as diluent and magnesium stearate as a lubricant was used. Powder mass was compressed into tablets using a 10 station rotary tablet punching press with a 12 mm punch and die set. Each tablet contained 15 mg of Pioglitazone. The diameter of all tablets was found to be 12 mm and thickness was in the range of 2.87 ± 0.08 to 2.97 ± 0.06 mm. It was evident from the friability (<1%) study, that all the tablets have sufficient strength indicating compliance with the Pharmacopoeial requirements. The density of all formulations below 1 gm/cm^3 indicated the density of formulations lower than gastric fluid. The hardness of tablets was found to be between 4.89 ± 0.16 to 5.24 ± 0.12 Kg indicating good strength. The prepared tablets had an average weight of in the range of 310± 0.2 to 320 ± 0.6 and in compliance with Indian Pharmacopoeial limits and none of the batches showed more than 5% of the average weight, indicating consistency in the preparation of the tablet with minimal batch to batch variation. The drug content analysis confirmed uniform dispersion of the drug in the tablets and it was well within the range of 96.71 ± 0.38-99.32 ± 0.51 % and also complies with the Pharmacopoeial limits.FT-IR spectral study results indicate that the drug and polymers were compatible with each other. The evaluation of thermograms obtained from DSC revealed that no interaction between the drug and the polymers from the evaluation of DSC thermograms. It was evident that no change in the melting point of Pioglitazone was evidenced even after it was formulated as a floating matrix tablet.

INTRODUCTION

The oral route is a widely accepted route of administration. The drug delivery systems designed to administer by oral route to enhance patient compliance. It is significantly impacting on healthcare economics. The major problem to attain significant therapeutic efficacy of drug molecules and potential agents like peptides, nucleic acid and proteins to manage the diverse diseases is the paucity of targeted drug delivery to cells. Conventional peroral dosage system is unable to attain prolongation of an effective bioavailability as well as plasma concentration. Due to the changing environment in the gastrointestinal tract (GIT), owing to several physiological barriers like gastric motility (GM), gastric residence time (GR), gastric emptying (GE), and stomach pH, etc. As a result, the need to develop a novel/new system for active therapeutic agents. One of the unique systems to overcome these barriers is gastroretentive drug delivery systems (GRDDS)[1,2]. Prolonged gastric retention increases bioavailability, decreases wastage of drugs, increases the solubility of drugs, which are less soluble in alkaline pH.[3] These dosage forms prolong the gastric residence time enabling an extended absorption phase for the local treatment of drugs and better bioavailability for the drugs that are unstable in the intestinal or colonic environment.[4,5] Gastric retention can be achieved by mucoadhesion or bio adhesion systems,[6] expansion systems,[7,8] high density systems,[9,10,11] magnetic systems,[12,13,14,] super porous hydrogels,[15,16] raft forming systems,[17,18,19] low density systems,[20,21,22] and floating ion exchange resins.[23]

Pioglitazone is an effective oral antidiabetic agent that belongs to the thiazolidinedione drug class. Pioglitazone belongs to BCS class II and exhibits low and variable oral bioavailability. It is majorly absorbed from stomach[24]. Pioglitazone has a short biological half-life of 3-5 h and is eliminated rapidly[25]. Hence controlled release floating formulations are needed for pioglitazone to improve its oral bioavailability and also to prolong its duration of action and to improve patient compliance.

MATERIALS AND METHODS

MATERIALS

Pioglitazone HCland low-density polypropylene foam powder (Accurel ® MP1000) was obtained as a gift sample from Ranbaxy Labs (Hyderabad, India) and Membrana GmbH, (Obernburg, Germany), respectively. Carrageenan gum, Aloe vera Gel powder, and

Magnesium stearate were obtained from Loba Chemie, Mumbai, India. All other reagents used in the present study were of analytical reagent grade.

METHODS

ANALYTICAL METHODS

Pioglitazone: The method described by Pawan K Basniwa was followed.[26]

Stock solution: Pioglitazone in pH 1.2 hydrochloric acid (HCl) buffer (100 µg/ml).

Scanning: From the stock solution, a suitable concentration (10 µg/ml) was prepared with pH 1.2 Hydrochloric acid buffer solution and a UV scan was taken between 200-400 nm. The spectrum is given in figure 1. The absorption maxima of 224 nm were selected and utilized for further studies.

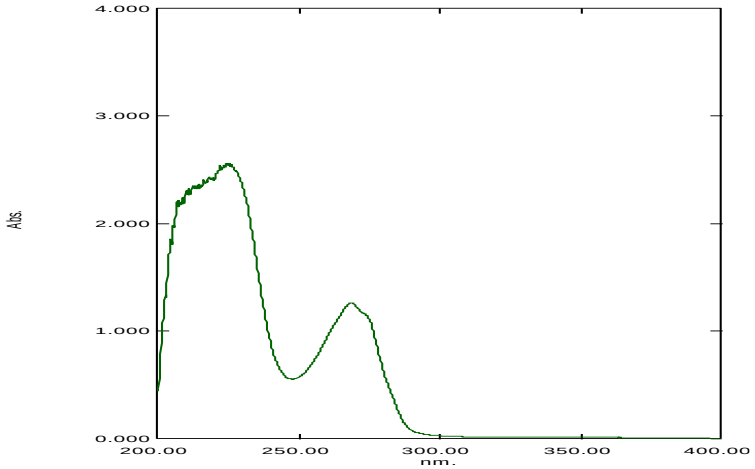


Figure No. 1: UV-Spectra of Pioglitazone in pH 1.2 hydrochloric acid buffer

Standard Plot: From the stock solution, 05,10, 15, 20, and 25 µg/ml solutions of Pioglitazone were prepared in pH 1.2 hydrochloric acid buffer solution. The absorbance was measured at 224 nm and a graph of concentration versus absorbance was plotted. Standard plot data of Pioglitazone in pH 1.2 hydrochloric acid buffer solution is reported in table 1 and graph in figure 2.

Table No. 1: Standard plot data for Pioglitazone in pH 1.2 hydrochloric acid buffer

Concentration (µg/ml)	Absorbance at 224 nm (mean ± SD*)
0	0
05	0.171± 0.000
10	0.342±0.070
15	0.508± 0.038
20	0.671± 0.102
25	0.837± 0.102

*Standard deviation, n = 3

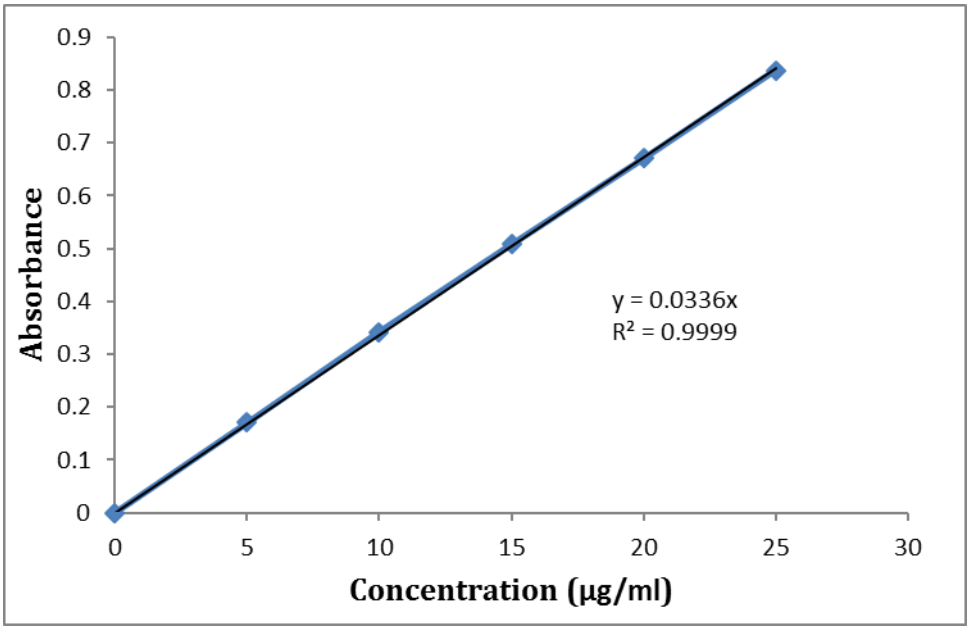


Figure No. 2: Standard plot for Pioglitazone in pH 1.2 hydrochloric acid buffer

Formulation of Non-Effervescent floating tablets[27, 28]

The non-effervescent Floating matrix tablets were prepared by direct compression method. All the ingredients were blended to get a homogenous mixture. Accurel® MP1000 as low-density polypropylene foam powder, Aloe vera gel powder as release retardant, Carrageenan gum as swellable polymer, lactose as diluent and magnesium stearate as a lubricant was used. Powder mass was compressed into tablets using a 10 station rotary tablet punching press with

a 12 mm punch and die set. Each tablet contained 15 mg of Pioglitazone Composition of each tablet is given in table 2.

Table No. 2: Formulation chart of non-effervescent floating Pioglitazone tablets

Ingredients (mg)	NF I	NF II	NF III	NF IV	NF V	NF VI	NF VII	NF VIII	NF IX
Pioglitazone	15	15	15	15	15	15	15	15	15
Accurel®MP1000	140	140	140	140	140	140	140	140	140
Aloevera Gel powder	45	55	65	45	55	65	45	55	65
Carrageenan gum	35	45	55	45	55	35	55	35	45
Lactose	76.5	56.5	36.5	66.5	46.5	56.5	56.5	66.5	46.5
Magnesium Stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Total Weight	315	315	315	315	315	315	315	315	315

Technological characteristics of floating tablets[29, 30]

Weight variation test

20 tablets from each formulation were randomly picked up and weighed individually and the average weight was calculated. The individual weights were then compared with the average weight.

$$\% \text{ deviation} = \frac{\text{Average weight of tablet} - \text{individual tablet weight}}{\text{Average weight of tablet}} * 100$$

Friability

Ten tablets were weighed and placed in a Roche friabilator and rotated at 25 rpm for 4 min. The tablets were taken out, de-dusted, and reweighed. The percentage friability of the tablets was calculated using the equation:

$$\% F = \{1-(W_f/W_o)\} \times 100$$

Where, % F is percentage friability, W_o is the initial weight of the tablet and W_f is the final weight of tablets after revolutions.

Compressed tablets with a loss of less than 1 % are generally considered acceptable.

Hardness

The hardness of core tablets was measured using Inweka hardness tester. A total of five tablets from each formulation were taken for the study and the average of the three is reported. It is expressed in kg.

Thickness and diameter

The thickness and diameter of the tablets were determined by using the Mitutoyo micrometer screw gauge. The average of five tablets from each formulation was taken. It is expressed in millimeters.

Uniformity of drug content

Drug content uniformity in the tablets was determined by randomly selecting 10 tablets that were powdered. The quantity equivalent to a single dose of the drug was dissolved in HCl buffer solution, pH 1.2 for 5 h with occasional shaking and diluted to 100 ml with buffer. After filtration to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with the buffer. The absorbance was measured at the required λ_{max} using a UV-visible spectrophotometer. The experiments were carried out in triplicate for all formulations and average values were recorded.

The drug content was calculated using the following equation:

% Drug content = Conc. (µg/ml) × Dilution factor × 100/ 50

Drug-excipient compatibility studies

Fourier transform infrared spectroscopy (FT-IR)

To evaluate the integrity and compatibility of the drug in the formulation, drug-excipient interaction studies were performed. Pure drug and optimized formulations were analyzed by Fourier transform infra-red (FTIR) spectroscopy. FTIR spectra of pure drug and its formulations were obtained by FT-IR Shimadzu 8400S (Japan) spectrophotometer using the KBr pellet method. The samples were scanned from 400 to 4,000 cm^{-1} wave number.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry was performed on a pure sample of drug and its formulation. Calorimetric measurements were made with empty cells (high purity alpha-alumina discs) as the reference. The dynamic scans were taken in a nitrogen atmosphere at the heating rate of 10 °C min^{-1}. The energy was measured as Joules per kilocalorie.

***In-vitro* floating studies[31]**

The *in-vitro* buoyancy was characterized by floating lag time and total floating time. The test was performed using a USP dissolution apparatus type-II (basket) using 900 ml of 0.1 N HCl buffer solution at 100 rpm at 37 ± 0.5°C. The time required for the formulation to rise to the surface of the dissolution medium and the duration for which the formulation constantly floated on the dissolution medium were noted as floating lag time and total time respectively.

Water uptake studies[32]

The swelling of the polymers was measured by their ability to absorb water and swell. The water uptake study of the tablet was done using a USP dissolution apparatus type-II (basket) in 900 ml of pH 1.2 Hydrochloric acid buffer at 100 rpm. The medium was maintained at 37 ± 0.5°C throughout the study. At regular time intervals, the tablets were withdrawn, blotted to remove excess water, and weighed. Swelling characteristics of the tablets were expressed in terms of water uptake (WU) as:

$$WU\ (\%) = \frac{\text{Weight of Swollen tablet- Initial weight of tablet}}{\text{Initial weight of tablet}} \times 100$$

***In-vitro* drug release study[33, 34, 35]**

The release rate of the drug from formulations was determined using USP dissolution testing apparatus II (basket type). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37± 0.5 ºC and 50 to 100 rpm. Aliquots (5mL) were withdrawn at regular intervals for 12 h, the sample was replaced by its equivalent volume of fresh dissolution medium to maintain the sink condition. The samples were analyzed UV-spectrophotometrically at a wavelength corresponding to the absorption maxima of the drugs. The release kinetics was fitted into various models using PCP dissolution v2.08 software.

Mechanism of drug release[36, 37,38,]

The different mathematical models may be applied for describing the kinetics of the drug release process from dosage forms the most suited being the one that best fits the experimental results. The best models describe drug release from pharmaceutical dosage form resulting from a simple phenomenon, or when this phenomenon, by being the rate-limiting step, conditions all the process occurring in the system. The kinetics of release from formulations were determined by finding the best fit of the release data to zero order, first order, matrix(Higuchi), Hixson-Crowell, and Korsmeyer- Peppas plots. Higuchi developed several theoretical models to study the release of high and low water-soluble drugs incorporated in the semi-solid and/or solid matrices. According to this model, drug release was described as a square root of the time-dependent diffusion process based on Fick's law. This relation can be used to describe drug dissolution from several types of modified release pharmaceutical dosage forms.

$$Q_t = K_H = \sqrt{t}$$

Where, K_H is Higuchi's rate constant, and $Q_t$is the amount of drug released at time *t*. If a plot of the square root of time versus cumulative amount of drug release yields a straight line, and the slope is 1 or more than 1, then the particular dosage form is considered to follow Higuchi kinetics of drug release. In some experimental situations, the release mechanism deviates from the Fick's equation, following an anomalous behavior (Non-Fickian release). In these cases, a more general equation can be used.

Korsmeyer et al. developed a simple, semi-empirical, relating exponentially the drug release to the lapsed time.

$$Q_t / Q_\alpha = Kt^n$$

Where, $Q_t/Q_\alpha$is the fraction of drug released at time *t*; *K* is the constant comprising structural and geometric characteristics of the tablets; and *n*, the release exponent, is a parameter that depends on the release mechanism and is thus used to characterize it.

Peppas used this *n* value to characterize different release mechanisms. If the *n* value is 0.5 or less, the release mechanism follows Fickian diffusion, and higher values ($0.5 < n < 1$) for mass transfer follow a non-Fickian model (anomalous transport).

Hixson-Crowell recognized that the area of the particle is proportional to the cubic root of its volume and derived an equation as follows:

$$W_o^{1/3} - W_t^{1/3} = Ks\ t$$

Where, Wo is the initial amount of drug, W_t is the remaining amount of drug in dosage form at time *t*, and K_S is a constant incorporating the surface volume relation.

Stability studies[39]

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. FDA and ICH specify the guidelines for stability testing of new drug products, as a technical requirement for the registration of pharmaceuticals for human use. The objective of stability testing is to investigate the effect of environmental factors on changes in product quality with time to establish its shelf life and recommend its storage conditions.

Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, leading to a lower concentration of the drug in the dosage form, hence the stability of pharmaceutical preparation needs to be evaluated. The objective of stability studies is to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperature and relative humidity (RH) conditions.

A drug formulation is said to be stable if it fulfills the following requirements:

- It contains at least 90% of the stated active ingredient.
- It contains an effective concentration of the added preservatives if any.
- It does not exhibit discoloration or precipitation, nor develops a foul odor.
- It does not develop irritation or toxicity.

Formulations were packed in a screw-capped bottle and studies were carried out for 12 months by keeping at:

- 25± 2°C and 60 ± 5% RH
- 30 ± 2°C and 65 ± 5% RH

and for 6 months at accelerated storage condition

- 40 ± 2°C and 75 ± 5% RH

Samples were withdrawn on 0, 3, 6 and 12 months for long term storage condition and 0, 3 and 6 months for accelerated storage condition and checked for changes in physical appearance and drug content as per ICH Q1A (R_2) guidelines. Graphs were plotted using Sigmaplot 12.0 to determine the statistical significance.

Results obtained in the methods and the conclusions arrived from them are provided in the following chapters.

RESULTS AND DISCUSSION

Technological characteristics of non-effervescent floating tablets

The results of the tablet evaluation parameters are presented in table 3. The diameter of all tablets was found to be 12 mm and thickness was in the range of 2.87 ± 0.08 to 2.97 ± 0.06 mm. It was evident from the friability (<1%) study, that all the tablets have sufficient strength indicating compliance with the Pharmacopoeial requirements. The density of all formulations below 1 gm/cm^3 indicated the density of formulations lower than gastric fluid. The hardness of tablets was found to be between 4.89 ± 0.16 to 5.24 ± 0.12 Kg indicating good strength. The prepared tablets had an average weight of in the range of 310± 0.2 to 320 ± 0.6 and in compliance with Indian Pharmacopoeial limits and none of the batches showed more than 5% of the average weight, indicating consistency in the preparation of the tablet with minimal batch to batch variation. The drug content analysis confirmed uniform dispersion of the drug in the tablets and it was well within the range of 96.71 ± 0.38-99.32 ± 0.51 % and also complies with the Pharmacopoeial limits.

Table No. 3: Physical properties of NEF tablets of Pioglitazone

*Standard deviation, n=3

Batch Code	Dimensions (mean ± SD*)		Friability (%) (mean ± SD*)	Density (g/cc) (mean ± SD*)	Hardness (Kg) (mean ± SD*)	Weight variation (mean ± SD*)	Drug content (%) (mean ± SD*)	Duration of buoyancy (h)
	Diameter (mm)	Thickness (mm)						
NEF I	12	2.87 ± 0.08	0.62 ± 0.01	0.893 ± 0.0020	4.89 ± 0.16	317 ± 0.2	97.81 ± 0.68	>12
NEF II	12	2.97 ± 0.06	0.67 ± 0.05	0.891 ± 0.0015	5.21 ± 0.13	320 ± 0.3	98.93 ± 0.64	>12
NEF III	12	2.91 ± 0.03	0.74 ± 0.08	0.892 ± 0.0017	5.16 ± 0.25	310 ± 0.2	98.24 ± 0.28	>12
NEF IV	12	2.93 ± 0.02	0.64 ± 0.07	0.888 ± 0.0016	5.24 ± 0.12	312 ± 1.1	99.32 ± 0.51	>12
NEF V	12	2.93 ± 0.06	0.68 ± 0.09	0.883 ± 0.0012	5.15 ± 0.18	319 ± 1.3	97.34 ± 0.52	>12
NEF VI	12	2.92 ± 0.04	0.62 ± 0.05	0. 892 ± 0.0017	4.99 ± 0.11	320 ±0.6	98.45 ± 0.21	>12
NEF VII	12	2.97 ± 0.04	0.65 ± 0.02	0. 891 ± 0.0025	5.16 ± 0.17	318 ±0.7	96.71 ± 0.38	>12
NEF VIII	12	2.96 ± 0.01	0.67 ± 0.01	0.872 ± 0.0037	5.14 ± 0.53	318 ± 1.1	98.20 ± 0.75	>12
NEF IX	12	2.95 ± 0.02	0.62 ± 0.04	0.892 ± 0.0014	5.19 ± 0.12	319 ± 0.8	98.27 ± 0.83	>12

Fourier transform infrared spectroscopy (FT-IR)

Pioglitazone and optimized formulation (NEF VI) were subjected to FT-IR spectrophotometric analysis, to find out interaction between the drug and the polymers employed in the preparation. The obtained spectra are shown in figure 3. Pioglitazone characteristic peaks were compared with the peaks of formulation NEF VI. The Pioglitazone characteristic bands were present and no major shift was observed when blended with polymers of floating matrix tablet. The results indicate that the drug and polymers were compatible with each other.

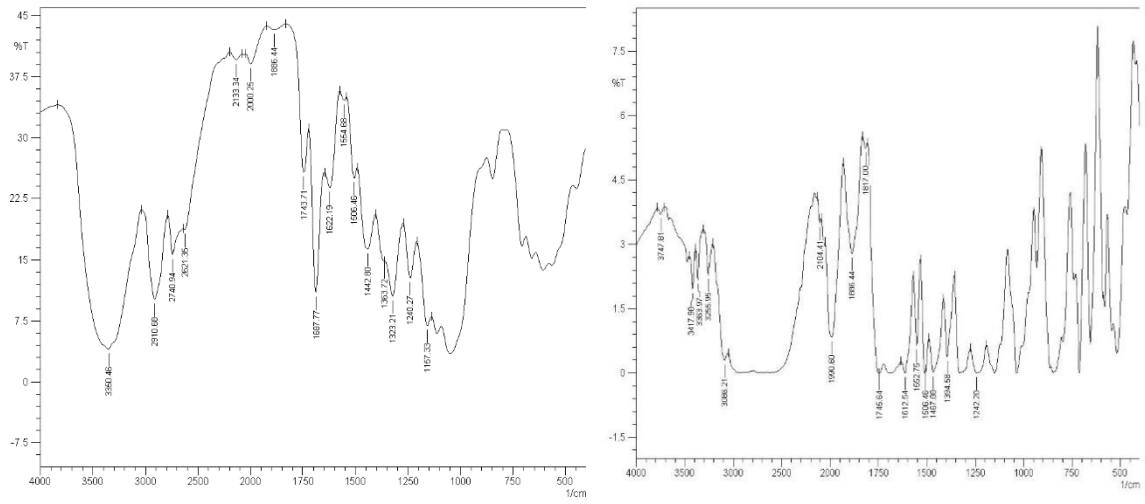


Figure No. 3: FTIR spectra of Pioglitazone& its tablet formulation NEF VI

5.3 Differential scanning calorimetry (DSC)

DSC study was carried out for Pioglitazone and formulation NEF VI and the obtained thermograms are shown in figure 4and the data is given in table 5.03. The Thermogram of Pioglitazone showed a sharp endothermic peak at 200^{o}C, corresponds to its melting point and formulation NEF VI showed an endothermic peak at 210^{o}C, which corresponds to the melting point of the Pioglitazone.

It was concluded that no interaction between the drug and the polymers from the evaluation of DSC thermograms. It was evident that no change in the melting point of Pioglitazone was evidenced even after it was formulated as a floating matrix tablet.

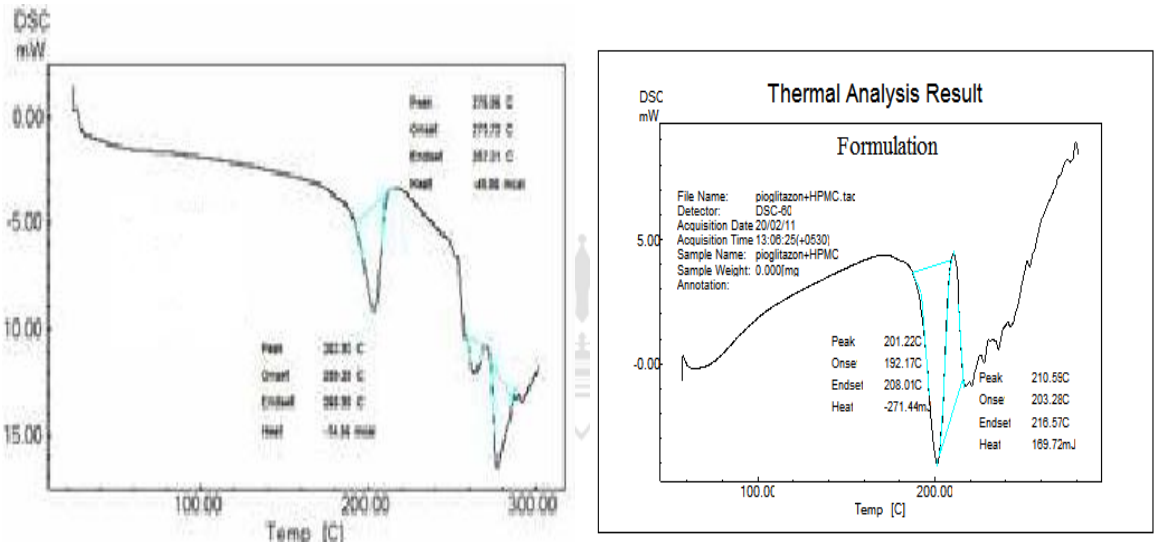
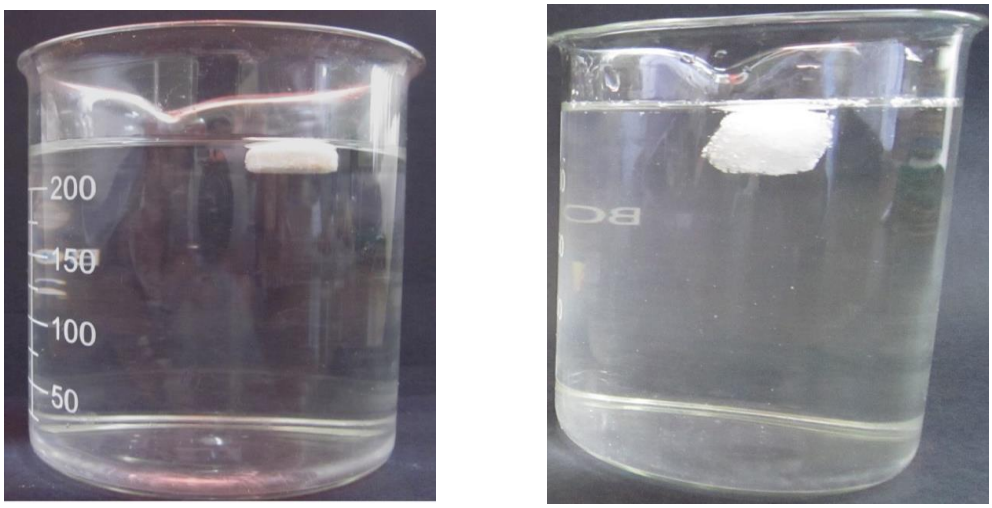


Figure No. 4: DSC thermograms of Pioglitazone& its floating matrix tablet formulation NEF VI

5.4 *In-vitro* floating studies

All the formulations showed well *in-vitro* buoyancy with no floating lag time (Zero) because of the presence of low-density polypropylene foam powder in the tablets. The tablets remained floated for more than 12 h to achieve gastric retention property. The photographs at different time intervals are given in figure 5.

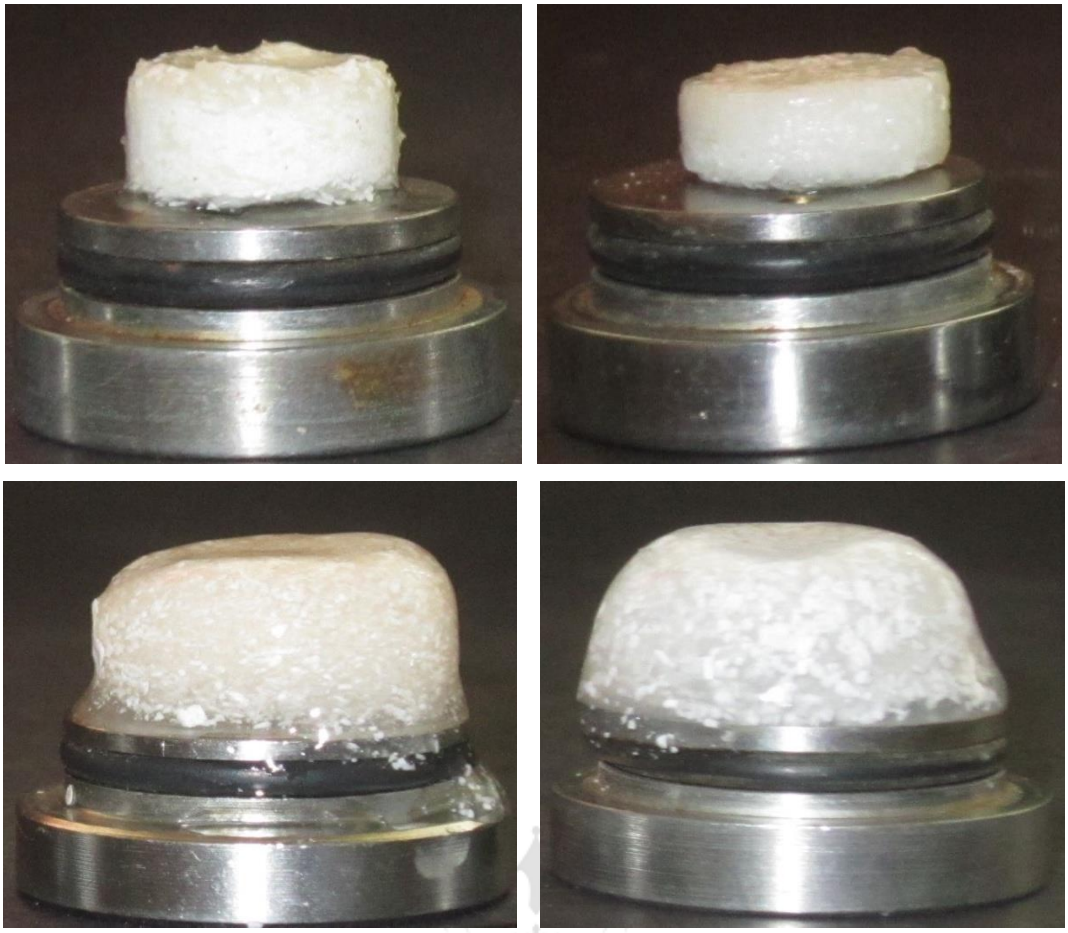


A) At zero time B) At 12th h

Figure No. 5: Picture of *in-vitro* floating behavior of tablet

Water uptake studies

The swelling behavior indicates the speed at which tablets absorb water from the dissolution medium and swell. Matrix tablets swelling increases with time because weight gain was increased proportionally with the rate of hydration up to 6 h and matrix appeared swollen almost from the beginning. Later on, swelling decreased due to the dissolution of the outermost gelled layer of tablets. The complete swelling was achieved by the end of 6 h. The swelling study was conducted and swelling photographs at 2nd and 8th hour time intervals are shown in figure 6& its profile is shown in figure 7. The swelling was directly proportional to the amount of Carrageenan gum and inversely related to the amount of Aloe vera Gel powder. The diffusion of the drug depends significantly on the water content of the tablet. This may be due to the mobility of the polymeric chains strongly depends on the water content of the system. Formulation NEF VI showed the lowest percentage of swelling because of the highest amount of Aloe vera Gel powder and the lowest amount of Carrageenan gum, whereas swelling was highest for formulation NEF VII due to lowest concentration of Aloe vera Gel powder and the highest concentration of Carrageenan gum. Drug release was proportional to the percentage of swelling.



A) At 1st h **B)** At 2nd h

C) At 2nd h **D)** At 8th h

Figure No. 6: Photographs showing swollen of floating matrix tablet

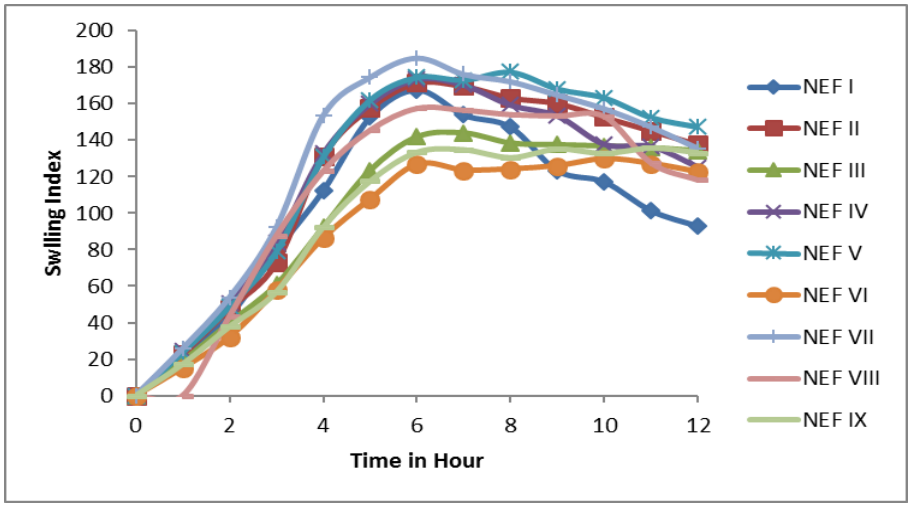


Figure No. 7: Swelling profile of floating matrix tablet formulations in pH 1.2 HCl buffer

5.6 *In-vitro* drug release studies

The release of the drug was dependent on the amount of Aloe vera Gel powder and Carrageenan gum. Drug release was found to be inversely related to the amount of release retardant (Aloe vera Gel powder) and proportional to the amount of swellable polymer (Carrageenan gum).

The *in-vitro* Pioglitazone release profile is depicted in figure 8. Data obtained showed that increased concentration of Aloe vera Gel powder and decreased amount of Carrageenan gum prolonged the drug release. Complete drug release was observed by the end of 12 h for formulation NEF VI due to the optimized concentration of Aloe vera Gel powder and Carrageenan gum (1:0.5), whereas the formulations NEF I, NEF IV and NEF VII showed complete release in 9 h because the amount of Carrageenan gum was high with the low amount of Aloe vera Gel powder. At the end of 10 h, 98.41 to 99.5 % drug release was observed for the formulations NEF II, NEF V, and NEF VIII. This was due to a further increase in the amount of Aloe vera Gel powder. With the same Carrageenan gum concentration, an increase in the amount of Aloe vera Gel powder led to a decrease in drug release. Drug release was directly proportional to the percentage of swelling. By comparing all formulations, NEF VI was considered as an optimized formulation that showed 99.35 % drug release at the end of 12 h. The formulation NEF III and NEF IX showed 99.10 and 99.15 % drug release at the end of 11 h.

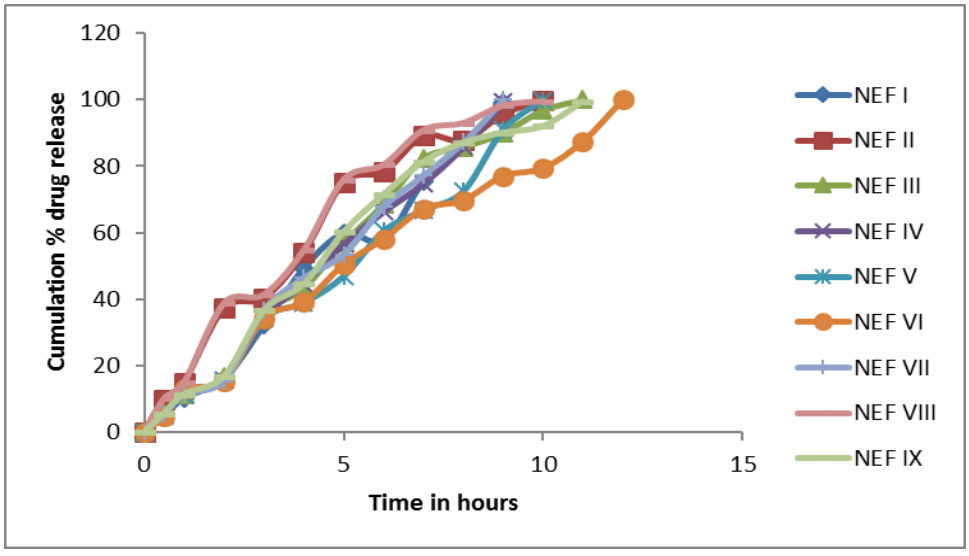


Figure No. 8: *In-vitro* drug release profile of Pioglitazone from floating matrix tablet formulations

Mathematical model fitting of obtained drug release data

In-vitro release studies data of floating matrix tablets were fitted into various mathematical models to determine the best-fit model. The best fit model with the highest correlation coefficient values or regression coefficients (R^2) for all the formulations is given in table 4. The results indicated that the best-fit model was found to be the Peppas model. When *in vitro* release data from the formulations was fitted to the Korsmeyer and Peppas equation, the release exponent values (n) obtained were <1 in all the cases. The n value ranged from 0.7745- 0.9709, hence the release mechanism was assumed to be anomalous transport.

Table No. 4: Data of various parameters of model fitting for non-effervescent floating matrix tablet formulations

Release Model		Batches								
		NEF I	NEF II	NEF III	NEF IV	NEF V	NEF VI	NEF VII	NEF VIII	NEF IX
Zero order	R^2	0.9936	0.9134	0.9716	0.9964	0.9926	0.9724	0.9954	0.9172	0.9547
First order	R^2	0.6818	0.8772	0.8525	0.5970	0.61637	0.658	0.7301	0.7735	0.8250
Hixson Crowell	R^2	0.8482	0.9773	0.9641	0.8321	0.8338	0.8889	0.8936	0.9643	0.9596
Matrix	R^2	0.8417	0.9496	0.9073	0.8632	0.8685	0.9220	0.8752	0.9492	0.9098
Peppas	R^2	0.9863	0.9816	0.9888	0.9865	0.9882	0.9874	0.9860	0.9789	0.9834
	n	0.9467	0.7755	0.9328	0.9719	0.9373	0.8852	0.9689	0.7828	0.9253
Best fit model		Zero order	Peppas	Peppas	Zero order	Zero order	Peppas	Zero order	Peppas	Peppas

5.9 Stability studies

The objective of stability studies is to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperature and RH. The optimized formulation of floating matrix tablets was subjected to stability studies according to ICH guidelines by storing at 25 ºC/60 % RH, 30 ± 2 ºC/65 RH, 30 ± 2 ºC/65 ± 5 % RH for 12 months and 40 ºC/75 % RH for 6 months. These samples were analyzed and checked for changes in physical appearance and drug content at regular intervals. The obtained data are presented in table 5. From the table, it was clear that the formulations did not undergo any chemical change/interaction during the study period.

Table No. 5: Stability study data of non-effervescent floating tablet (NEF VI) of Pioglitazone

Stability condition	Sampling interval (Months)	Physical appearance	% Drug content NEF VI (Mean ±SD*)
25 ± 2 ºC/60 ± 5 % RH	0	No change	98.42 ± 0.02
	3	No change	98.28 ± 0.08
	6	No change	98.24 ± 0.10
	12	No change	98.08 ± 0.10
30 ± 2 ºC/65 ± 5 % RH	0	No change	98.42 ± 0.11
	3	No change	98.03 ± 0.15
	6	No change	97.79 ± 0.08
	12	No change	97.51 ± 0.01
40 ± 2 ºC/75 ± 5 % RH	0	No change	98.42 ± 0.13
	3	No change	97.20 ± 0.18
	6	No change	96.17 ± 0.19

*Standard deviation, n=3

CONCLUSION

The non-effervescent Floating matrix tablets were prepared by direct compression method. All the ingredients were blended to get a homogenous mixture. Accurel® MP1000 as low-density polypropylene foam powder, Aloe vera gel powder as release retardant, Carrageenan gum as swellable polymer, lactose as diluent and magnesium stearate as a lubricant was used. Powder mass was compressed into tablets using a 10 station rotary tablet punching press with a 12 mm punch and die set. Each tablet contained 15 mg of Pioglitazone. The diameter of all tablets was found to be 12 mm and thickness was in the range of 2.87 ± 0.08 to 2.97 ± 0.06 mm. It was evident from the friability (<1%) study, that all the tablets have sufficient strength indicating compliance with the Pharmacopoeial requirements. The density of all formulations below 1 gm/cm^3 indicated the density of formulations lower than gastric fluid. The hardness of tablets was found to be between 4.89 ± 0.16 to 5.24 ± 0.12 Kg indicating good strength. The prepared tablets had an average weight of in the range of 310± 0.2 to 320 ± 0.6 and in compliance with Indian Pharmacopoeial limits and none of the batches showed more than 5% of the average weight, indicating consistency in the preparation of the tablet with minimal batch to batch variation. The drug content analysis confirmed uniform dispersion of the drug

in the tablets and it was well within the range of 96.71 ± 0.38-99.32 ± 0.51 % and also complies with the Pharmacopoeial limits.FT-IR spectral study results indicate that the drug and polymers were compatible with each other. The evaluation of thermograms obtained from DSC revealed that no interaction between the drug and the polymers from the evaluation of DSC thermograms. It was evident that no change in the melting point of Pioglitazone was evidenced even after it was formulated as a floating matrix tablet.

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