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# Formulation and Evaluation of Sustained Release Dual Matrix Tablets Using Compritol 888 ATO for Diabetes

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## Abstract

Recent developments in sustained-release drug delivery systems (SRDDS) aim to improve patient compliance while improving the safety and efficacy of the drug molecule by developing a convenient dose form. In the current research, the tablet was formulated with immediate-release granules of pioglitazone and sustained-release granules of caffeine. Sustained release granules for tablets were prepared using Compritol 888 ATO polymer in ratio with PVP (K30 and K90) that retard the release of drug from the tablet and for improvement of patient compliance. The sustained-release tablets were prepared by the wet granulation method. The formulated tablet was subjected to tests like thickness, friability, weight variation, hardness, drug content, in-vitro release study, and stability study. A drug and polymer compatibility study were performed by FTIR. Out of all the batches prepared the optimized batch (B4) is selected based on the concentration of Compritol 888 ATO with PVP-K90 is increased it showed better drug release as Compritol 888 ATO is a release retardant. The in-vitro drug release was found to be more than 90% after 12 hours. This release retardant (Compritol 888 ATO) at the optimized concentration formed a desired matrix with the PVP it showed and action with the combination of pioglitazone and caffeine proved to be a promising approach to antidiabetic action.

**Keywords:** Caffeine, Pioglitazone HCL, Sustained Release, Immediate Release and Matrix tablet.

## 1. Introduction

To improve selectivity and extend the duration of effect, sustained release dosage forms are intended to supplement the drug's pharmacological activity. Drug adverse effects and dosage frequency can be decreased with the use of sustained release preparations, which also enhance patient convenience. Incorporating drug molecules in slowly evaporating or inert porous materials makes it reasonably simple to create sustained release matrix tablets. Incorporating a drug release modulator into a matrix system is the most used technique [1, 2].

Sustained release dosage form is defined as a well characterized and reproducible dosage form, which is designed to control drug release profile at a specified rate to achieve desired drug concentration either in blood plasma or at target site [3]. This system will provide actual therapeutic control that would be temporal (time related), spatial (site related) or both [4]. Matrix tablet is defined as an "Oral solid dosage form in which active pharmaceutical ingredient is uniformly dispersed throughout polymeric matrices (hydrophilic or hydrophobic) which retards the drug release rate. This approach is widely used for formulating sustained release tablets [5].

The sustained release dual matrix tablet is a biphasic delivery system that aims to deliver drugs at two different rates or simultaneously releases two drugs with the following benefits, formulating two chemically compatible drugs into a system, simultaneously releasing two active pharmaceutical ingredients (APIs) with desired release profiles, increasing the efficacy of API by a synergistic effect, decreasing the dosing unit burden and better patient compliance.

Caffeine (1,3,7-trimethylxanthine) is a plant alkaloid with a chemical structure of C8H10N4O2 and a molecular weight of 194.19. It is a BCS class I drug having high solubility and permeability. In pure form, it is a bitter white powder. Structurally, caffeine (and the other methylxanthines) resembles the purines. The half-life of caffeine in the plasma of healthy individuals is about 5 hours, while the total plasma clearance rate for caffeine is estimated to be 0.078 L/h/kg [6].

Pioglitazone hydrochloride is a thiazolidinedione antidiabetic agent that decreases insulin resistance in the periphery and liver, resulting in increased insulin-dependent glucose disposal and decreased hepatic glucose output respectively. pioglitazone hydrochloride is indicated as monotherapy in patients not controlled by diet and exercise alone, to de-

crease blood glucose levels in patients with type 2 diabetes mellitus. It is mostly used in combination with other drugs. It is BCS Class II drug having low solubility and high permeability. Pioglitazone hydrochloride is a potent and highly selective agonist for peroxisome proliferator-activated receptor-gamma (PPARγ). PPARγ receptors are found in tissues important for insulin action such as adipose tissue, skeletal muscle, and liver. Activation of PPARγ nuclear receptors modulates the transcription of several insulin responsive genes involved in the control of glucose and lipid metabolism and the maturation of preadipocytes, predominantly of subcutaneous origin [7].

## 2. Materials

Pioglitazone HCL was obtained as gift sample from FDC and Caffeine from Medley Pharmaceuticals and Compritol 888 ATO from Gattefosse. Excipients and solvents was obtained from Vishal Chem India.

### 2.1. Methods

Matrix tablets, each containing 150 mg of Caffeine and 15 mg Pioglitazone HCl were prepared by a conventional non-aqueous wet granulation technique for sustained release granules and a direct compression technique for immediate release granules. The composition of various formulations of the tablets with their codes is listed in Table 1. The composition with respect to polymer combination was selected on the basis of trial preparation of tablets.

A batch of 30 tablets was prepared with each formula. For sustained release granules the ingredients were passed through a 60-mesh sieve. A blend of all ingredients except glidant and lubricant was mixed, particular attention had been given to ensure thorough mixing with a granulating agent. Granulation was done manually with a solution of isopropyl alcohol. The wet masses were passed through a 12-mesh sieve and the wet granules produced were first air dried for 10 min and finally at 45-50o in a hot air oven for 15-20 mins. The dried granules were sized by a 16-mesh sieve and after lubrication with magnesium stearate.

For an immediate release blend, all ingredients were passed through a 60-mesh sieve and mixed in geometric proportion.

**Table 1: Composition of Various Trial Formulations Prepared.**

| Name Of Ingredients | B1 | B2 | B3 | B4 | B5 | B6 | B7 | B8 | B9 | B10 | B11 | B12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SR Granules (mg) | | | | | | | | | | | | |
| Caffeine | 147 | 147 | 147 | 147 | 147 | 147 | 147 | 147 | 147 | 147 | 147 | 147 |
| Compritol 888 ATO | 240.35 | 227.7 | 215.05 | 202.4 | 189.7 | 177.1 | 240.35 | 227.7 | 215.05 | 202.4 | 189.7 | 177.1 |
| PVP K90 | 12.65 | 25.3 | 37.95 | 50.6 | 63.25 | 75.9 | - | - | - | - | - | - |
| PVP K30 | - | - | - | - | - | - | 12.65 | 25.3 | 37.95 | 50.6 | 63.25 | 75.9 |
| Isopropyl Alcohol | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S |
| Mg Stearate | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % |
| Talc | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % | 1 % |
| IR Granules (mg) | | | | | | | | | | | | |
| Pioglitazone Hcl | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| Caffeine | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| MCC | 78 | 76 | 74 | 72 | 78 | 77 | 76 | 75 | 79 | 77 | 75 | 73 |
| Sodium Starch Glycolate | 2 | 4 | 6 | 8 | - | - | - | - | - | - | - | - |
| Croscarmellose sodium | - | - | - | - | 2 | 3 | 4 | 5 | - | - | - | - |
| Crospovidone | - | - | - | - | - | - | - | - | 1 | 3 | 5 | 7 |
| Mg Stearate | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Talc | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

## Pre-Compression Characterization

***Organoleptic Properties:*** A small amount of sample is examined by simple visualization and colour, texture etc. were determined [7].

## Solubility Studies

A small quantity of the drug sample was taken in a test tube and the solubility was determined by European pharmacopoeia method [7].

## Bulk Density (ρB)

Bulk density is determined by a constant mass method using a measuring cylinder. The bulk density of a powder is the ratio of the mass of an untapped powder sample to its volume, including the contribution of the inter-particulate void volume. It is expressed in gm/ml and is given by

Bulk density (ρB) = M/Vo
Where, M = mass of the powder (weight taken in g)
Vo = Void volume (Untapped Volume in ml)

## Tapped Density (ρT)

Taped volume is measured by taping measuring cylinder till there is no change of reading [7]. It is expressed in gm/ml and is given by

Tapped density (ρT) = M/Vf
Where M = mass of the powder (weight taken in g)
Vf= Tapped Volume (Final bulk volume after tapped in ml)

Hausner Ratio
Hausner ratio is an indirect index to predict of powder flow. It is calculated by the following formula [7].

Hausner ratio = Tapped density (ρT)/Bulk density (ρB)
Hausner ratio is also calculated by following the formula
Hausner ratio = Vo/Vf

## Compressibility Index (Carr's Index)

Compressibility index (Carr's index) is an indirect parameter to assume flow property of powder. The compressibility index is determined by measuring the initial volume (Vo) and final volume (Vf) after complete tapings of powder sample in a measuring cylinder [7].

Compressibility index (CI) =(Vo–Vf)/Vo X 100
Alternatively, the compressibility index may be calculated using measured values for bulk density (ρB) and tapped density (ρT) as follows.

Compressibility index = 100 x {(ρT-ρB)/ρT}

## Angle of Repose

The angle of repose is the three-dimensional angle (relative to the horizontal base) assumed by a cone-like pile of material formed by different methods. The method is the fixed height method. In the fixed funnel, the method employs a funnel that was secured with its tip at a given height (2 cm), above the graph paper that was placed on a flat horizontal surface. Granules were carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. Thus, with r being the radius of the base of the conical pile. The angle of repose is calculated using the formula [7].

Tan θ = h/r
Where, h = height of the powder pile
r = radius of pile circle

## Absorption spectra of Caffeine and Pioglitazone HCL

The absorption spectra were prepared using 0.1N HCl, in the range of 200-400 nm. Calibration curve of Caffeien and Pioglitazone HCl [5] It was prepared by using a UV spectrophotometer (Shimadzu UV spectrophotometer) [8]. For this 100 mg each of the drug was dissolved in 0.1N HCl separately and shaken for complete dissolve. Then it was filtered, and dilution was done to form a 10-ppm solution of each. The sample was analyzed under a UV spectrophotometer for spectrum.

## FTIR Study

The infrared spectrum was taken for the pure Caffeine and Pioglitazone HCl, PVP and Sodium Starch Glycolate [9]. FT-IR studies were carried out by the KBr disk method using computer-mediated Fourier transformed infrared spectroscopy (FTIR)

## Post-Compression Characterization

***Appearance:*** Prepared tablets were observed and determined for any physical appearance including elegance, shape, colour, and surface textures [10].

### 2.2. Dimensional Analysis

Dimensional analysis includes the Thickness of tablets that were determined using AEROSPACE digital vernier calliper. Randomly three tablets select from each batch and average values are calculated [10].

## Hardness

Hardness is measuring the force required to break the tablet. The test was performed using a VINSYST digital portable hardness tester (VTHT-500). The hardness of 3 tablets from a batch are determined. Hardness is measured in kg/cm2 [10].

## Weight Variation Test

Weight variation test is carried out by taking Individual weights of 20 tablets randomly from the whole batch. Individual weights were then compared with the average weight for the weight variations [10].

PD = [(Wavg–Winitial)/(Wavg)] x 100

Where,
PD = Percentage deviation,
Wavg = Average weight of the tablet,
Winitial = Individual weight of the tablet.

## Friability Test

10 tablets were accurately weighed and placed in the drum.

Rotate the drum 100 times which means 25±1 rpm for 4 min and remove the tablets. Remove any loose dust from the tablets and accurately weighed them. A maximum mean mass loss from the three samples of not more than 1.0% is acceptable [10].

% friability = (Initial weight-final weight)/Initial weight x 100

## Disintegration Test

Time for the formulated Tablets was assessed using the disintegration apparatus. Six Tablets were placed in six tubes of the basket rack assembly, and the apparatus was operated using 0.1N HCL at 37 ± 2°C. The Tablets were observed, and the time taken for complete disintegration of all tablets was recorded [10].

## Drug Content

5 tablets were powdered, and 100 mg of drug equivalent powder was dissolved in buffer pH 7.5. The volume of the solution is made up to 100 ml by that media. The solution was filtered and diluted 100 times and analysed spectrophotometrically (Shimadzu, Model no: UV 1800240V) and further calculations were carried out to determine drug content in one tablet [10].

## In Vitro Drug Release Study

Those tests were carried out using dissolution test apparatus containing a specified volume of 900 ml of 0.1N HCL and after 2 hrs. Phosphate buffer (pH 6.8) was used [10]. The temperature was maintained at 37±0.50C. The tablets are directly placed in a medium and immediately the paddles were started at the specified rate (75 RPM). Within the time interval specified (0.3,1,2,3,4,6,8,10,12,14 hrs.), 5 ml of sample are withdrawn and for immediate release Pioglitazone HCL time interval (5,10,15,30,45 mins) 5 ml of sample are withdrawn separately. The samples were filtered and from the filtrate 1 ml was diluted to 10 ml. These samples are analyzed, and further calculation is carried out to get drug release. The drug release data were plotted and tested (Cumulative % drug released Vs time).

**Table 2: Preformulation Results**

| Parameter | Pioglitazone HCL | Caffeine |
|---|---|---|
| Colour | White | White |
| Odour | characteristic odour | characteristic odour |
| Texture | Smooth | Smooth |
| Solubility | Soluble in warm water and freely soluble in methanol, Dimethylformamide and 0.1 N HCL. | Insoluble in water, freely soluble in methanol, Dimethylformamide and 0.1 N HCL. |
| Absorption spectra | 220 nm | 273 nm |

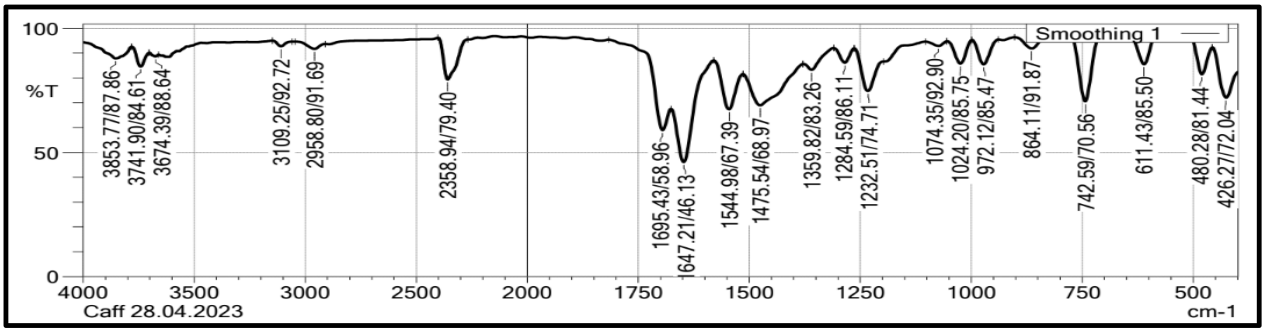


**Figure 1:** FTIR spectrum of Caffeine

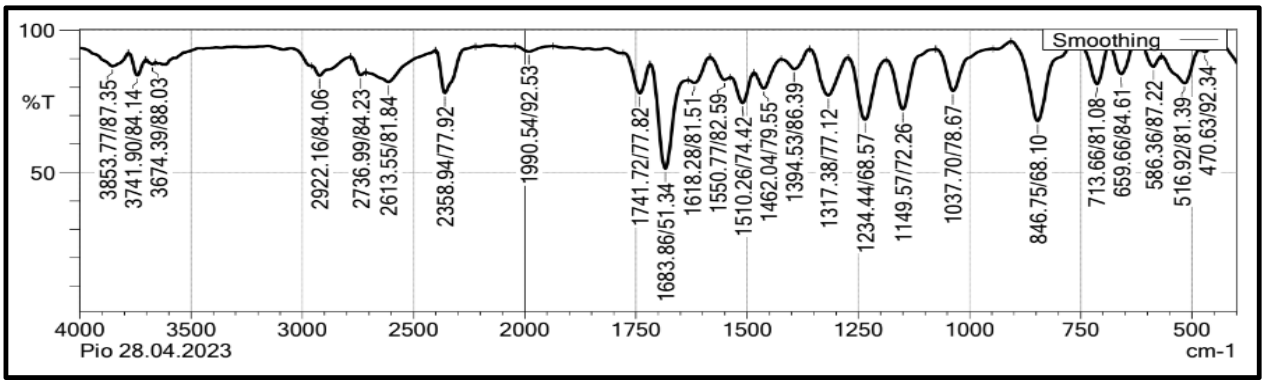


**Figure 2:** FTIR spectrum of Pioglitazone HCL



**Citation:** Ahuja, A., Nida, M. A., Al-Sayigh, F. A. R., Nazmi, A. S., Al-Humaid, S. H., et al. (2024). Formulation and Evaluation of Novel Drug Delivery System Using in Situ Gelling Approach for Antiemetic Drugs Used in Cancer Patients. Pharma Research Journal, 1(1). 1-5.

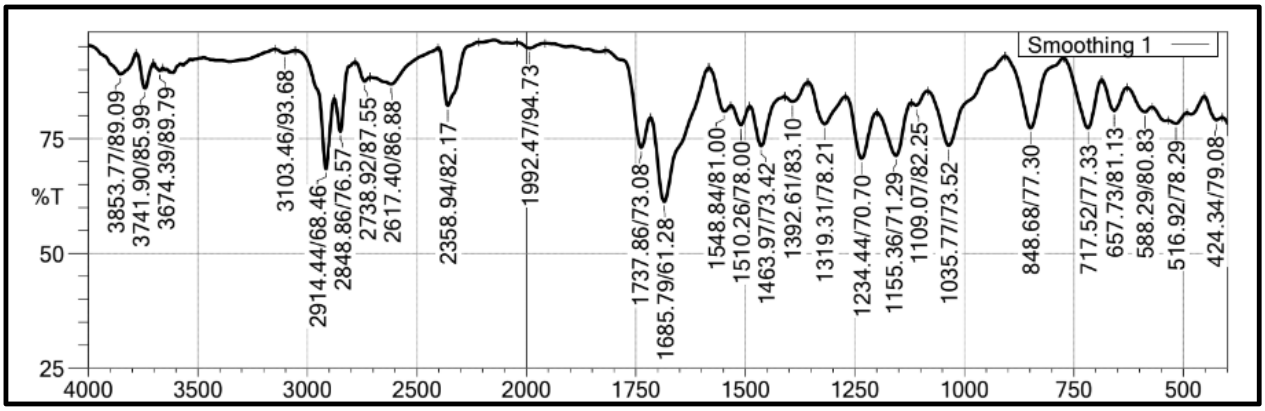


**Figure 3:** FTIR spectrum of Tablet formulation

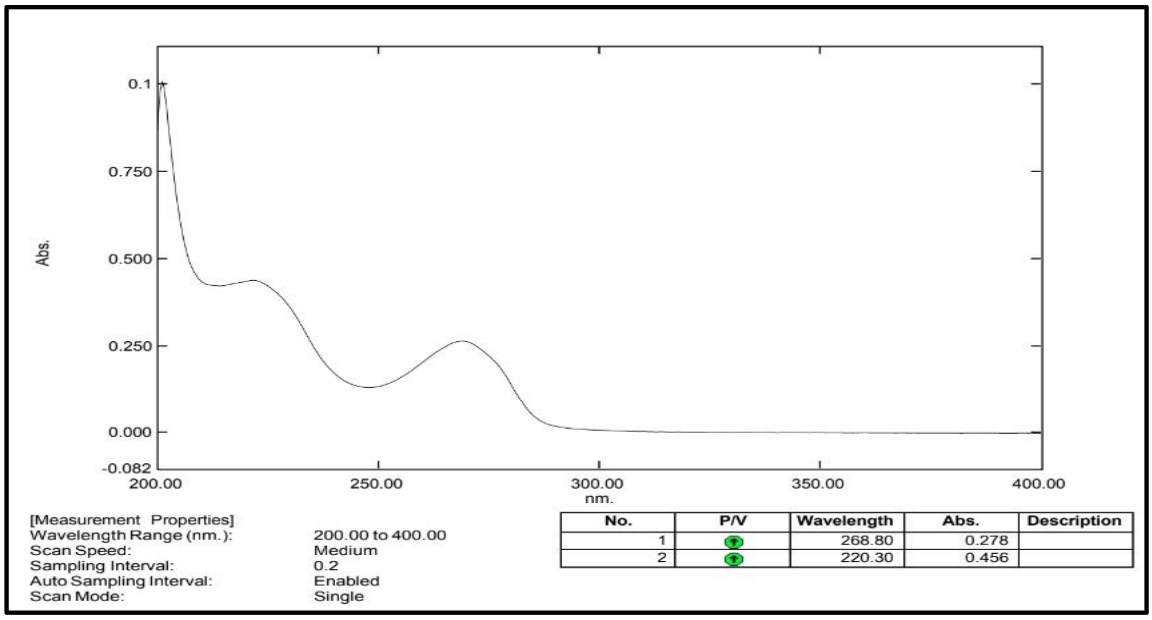


**Figure 4:** Absorption spectrum of Pioglitazone HCL

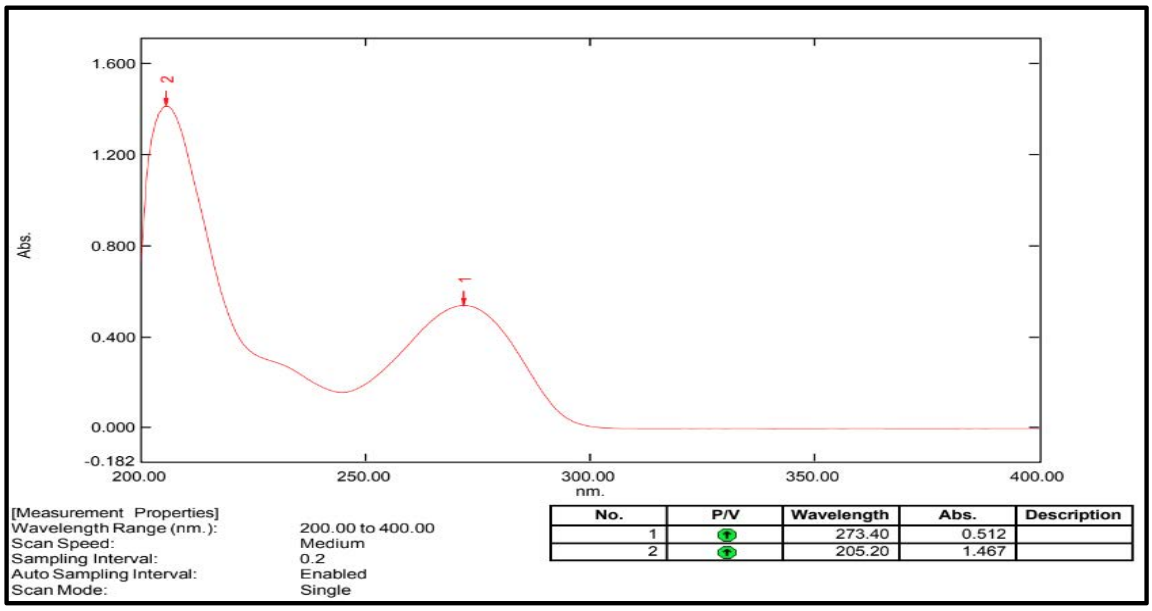


**Figure 5:** Absorption spectrum of Caffeine

**Table 3: Pre-compression results of sustained release blend**

| Formulation Code | Angle of Repose (g/ml) | Bulk Density (g/ml) | Tapped Density | Carr's Index | % Compressibility | Hausner's Ratio |
|---|---|---|---|---|---|---|
| B1 | 32.61° | 0.36 | 0.4321 | 0.1668 | 16.685 | 1.200 |
| B2 | 31.75° | 0.376 | 0.489 | 0.2310 | 23.1083 | 1.300 |
| B3 | 29.66° | 0.46 | 0.574 | 0.1986 | 19.860 | 1.247 |
| B4 | 34.78° | 0.44 | 0.484 | 0.0909 | 9.090 | 1.1 |
| B5 | 34.78° | 0.437 | 0.601 | 0.2728 | 27.287 | 1.375 |
| B6 | 31.16° | 0.474 | 0.542 | 0.1254 | 12.546 | 1.143 |
| B7 | 33.22° | 0.401 | 0.4819 | 0.1678 | 16.787 | 1.201 |
| B8 | 33.4° | 0.399 | 0.499 | 0.2004 | 20.040 | 1.250 |
| B9 | 32.55° | 0.394 | 0.437 | 0.0983 | 9.839 | 1.109 |
| B10 | 35.56° | 0.455 | 0.52 | 0.125 | 12.5 | 1.142 |
| B11 | 32.61° | 0.44 | 0.565 | 0.2212 | 22.123 | 1.284 |
| B12 | 29.87° | 0.437 | 0.567 | 0.2292 | 22.927 | 1.297 |

**Table 4: Pre-compression results of immediate release blend**

| Formulation Code | Angle of Repose (g/ml) | Bulk Density (g/ml) | Tapped Density | Carr's Index | % Compressibility | Hausner's Ratio |
|---|---|---|---|---|---|---|
| B1 | 29.41 | 0.2 | 0.236 | 0.1525 | 15.254 | 1.18 |
| B2 | 28.45 | 0.21 | 0.247 | 0.1497 | 14.979 | 1.176 |
| B3 | 31.24 | 0.19 | 0.201 | 0.0547 | 5.472 | 1.057 |
| B4 | 29.44 | 0.18 | 0.214 | 0.1588 | 15.887 | 1.1888 |
| B5 | 31.49 | 0.17 | 0.223 | 0.2376 | 23.766 | 1.3117 |
| B6 | 32.45 | 0.22 | 0.245 | 0.1020 | 10.204 | 1.113 |
| B7 | 27.25 | 0.21 | 0.244 | 0.1393 | 13.934 | 1.161 |
| B8 | 26.25 | 0.17 | 0.234 | 0.2735 | 27.350 | 1.376 |
| B9 | 28.55 | 0.18 | 0.214 | 0.1588 | 15.887 | 1.1888 |
| B10 | 29.63 | 0.19 | 0.245 | 0.2244 | 22.448 | 1.289 |
| B11 | 29.85 | 0.21 | 0.233 | 0.0987 | 9.871 | 1.109 |
| B12 | 27.12 | 0.22 | 0.254 | 0.1338 | 13.385 | 1.154 |

**Table 5: Post-compression results**

| Formulation Code | Thickness | Hardness | Friability (%) | Weight Variation | Drug content | |
|---|---|---|---|---|---|---|
| | | | | | Caffeine | Pioglitaone HCL |
| AT1 | 3.94 ± 0.03 | 7.36 ± 0.02 | 0.47 | 497.95 ± 9.29 | 97.13 | 98.31 |
| AT2 | 4.16 ± 0.03 | 7.66 ± 0.02 | 0.44 | 498.4 ± 5.17 | 96.92 | 100.48 |
| AT3 | 4.08 ± 0.02 | 7.6 ± 0.05 | 0.46 | 504.55 ± 4.69 | 98.80 | 102.65 |
| AT4 | 4.02 ± 0.01 | 7.89 ± 0.08 | 0.4 | 494.85 ± 7.70 | 100.06 | 99.75 |
| AT5 | 4.13 ± 0.05 | 7.84 ± 0.05 | 0.66 | 491.45 ± 8.10 | 98.38 | 99.27 |
| AT6 | 4.06 ± 0.04 | 7.89 ± 0.07 | 0.34 | 493.95 ± 9.31 | 97.55 | 99.75 |
| AT7 | 4.14 ± 0.03 | 7.92 ± 0.06 | 0.42 | 493.9 ± 10.70 | 96.92 | 101.20 |
| AT8 | 4.05 ± 0.03 | 8.25 ± 0.04 | 0.39 | 492.4 ± 9.95 | 100.2 | 97.83 |
| AT9 | 4.25 ± 0.03 | 8.12 ± 0.02 | 0.32 | 487.8 ± 5.74 | 98.17 | 102.16 |
| AT10 | 4.13 ± 0.03 | 8.15 ± 0.05 | 0.51 | 489 ± 5.48 | 100.48 | 103.85 |
| AT11 | 4.23 ± 0.02 | 8.05 ± 0.03 | 0.57 | 494.5 ± 9.75 | 101.31 | 102.89 |
| AT12 | 4.03 ± 0.03 | 8.11 ± 0.07 | 0.4 | 489.3 ± 7.73 | 99.64 | 101.92 |

**Table 6: Drug Release of Caffeine**

| TIME (Hrs) | B1 | B2 | B3 | B4 | B5 | B6 | B7 | B8 | B9 | B10 | B11 | B12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 6.45 | 5.66 | 6.07 | 5.28 | 6.07 | 5.25 | 2.65 | 4.42 | 4.94 | 5.32 | 4.53 | 5.25 |
| 1 | 9.24 | 10.89 | 10.29 | 11.75 | 10.29 | 8.44 | 7.48 | 10.20 | 11.52 | 12.51 | 12.05 | 12.84 |
| 2 | 20.55 | 16.26 | 19.91 | 19.92 | 19.91 | 20.81 | 14.96 | 16.86 | 16.27 | 16.65 | 16.31 | 16.27 |
| 3 | 26.64 | 31.39 | 29.12 | 36.08 | 29.12 | 26.41 | 23.82 | 24.81 | 23.86 | 24.69 | 24.96 | 24.95 |
| 4 | 32.81 | 41.72 | 40.88 | 50.03 | 40.88 | 38.27 | 34.71 | 42.32 | 34.30 | 35.62 | 42.33 | 36.04 |
| 6 | 48.28 | 50.66 | 52.05 | 63.33 | 52.05 | 49.21 | 46.97 | 57.56 | 41.89 | 45.70 | 46.94 | 46.15 |
| 8 | 55.82 | 61.60 | 63.11 | 73.23 | 63.11 | 58.92 | 58.56 | 71.05 | 49.95 | 54.11 | 52.84 | 52.99 |
| 10 | 66.60 | 76.53 | 77.52 | 83.64 | 77.52 | 69.89 | 68.98 | 76.47 | 59.11 | 65.08 | 61.65 | 64.74 |
| 12 | 80.06 | 86.86 | 82.23 | 88.21 | 82.23 | 78.69 | 75.10 | 74.81 | 70.04 | 74.67 | 69.30 | 74.18 |
| 14 | 87.06 | 92.04 | 90.32 | 96.98 | 90.32 | 92.44 | 83.16 | 84.78 | 78.91 | 81.09 | 77.21 | 78.71 |

**Table 7: Drug release of Pioglitazone HCL**

| TIME (Mins) | B1 | B2 | B3 | B4 | B5 | B6 | B7 | B8 | B9 | B10 | B11 | B12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 19.95 | 25.59 | 31.66 | 37.73 | 35.57 | 36.43 | 34.27 | 37.73 | 22.99 | 19.95 | 21.69 | 25.59 |
| 10 | 30.47 | 34.84 | 43.55 | 57.03 | 48.78 | 49.21 | 47.47 | 50.96 | 26.59 | 47.82 | 47.40 | 49.59 |
| 15 | 41.37 | 47.90 | 52.29 | 69.71 | 58.82 | 59.69 | 57.95 | 60.57 | 56.53 | 58.82 | 59.68 | 60.13 |
| 30 | 62.69 | 69.23 | 74.02 | 84.53 | 64.95 | 67.13 | 69.72 | 72.33 | 71.45 | 70.16 | 69.29 | 74.07 |
| 45 | 73.65 | 78.02 | 82.39 | 95.89 | 74.09 | 76.71 | 78.02 | 81.07 | 76.73 | 75.42 | 81.06 | 84.12 |

## 3. Results and Discussion

The tablet was prepared and evaluated for various parameters. The pre-compression and post-compression parameters were obtained and were within the acceptable limits of the pharmacopoeial specification. Both the drugs itself was a crystalline powder, the colour is off white and it is odourless. FTIR studies showed there was no interaction between both the drug and with the excipients and found out to be stable. In the post formulation evaluation, it was found that all the tablets were within the range of pharmacopoeial standards. The hardness of all the formulation was found to be in good mechanical strength ranging from 7.36 to 8.11 kg/cm2. The weight variation was found in all designed formulations in the range of 489 to 504 mg. The friability of all the formulations was within the approved range (<1%). Drug content was in the range between 96.92%-101.31% for Caffeine and 98.31 - 103.55 for Pioglitazone HCl respectively which are within the limits. The B4 batch was selected as the best batch as it has the highest Drug release for both of the drugs within the stipulated time period (Figure 7 and 8).

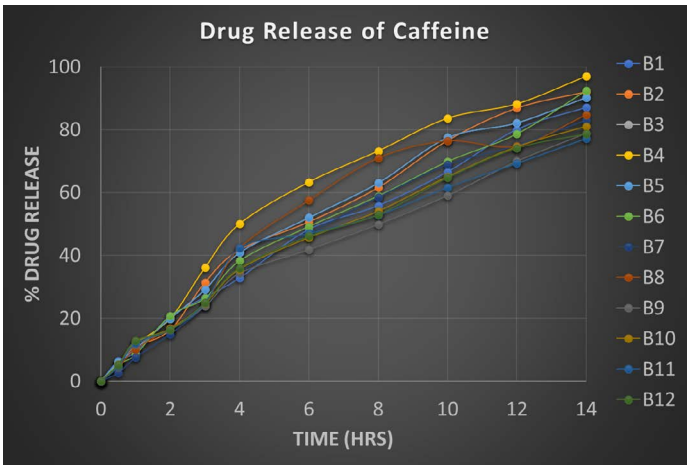


**Figure 7:** Drug release profile of Caffeine (Batch 1-12)


*Citation:* Ahuja, A., Nida, M. A., Ai-Sayigh, F. A. R., Nazmi, A. S., Ai-Humaid, S. H., et al. (2024). Formulation and Evaluation of Novel Drug Delivery System Using in Situ Gelling Approach for Antiemetic Drugs Used in Cancer Patients. Pharma Research Journal, 1(1). 1-5.

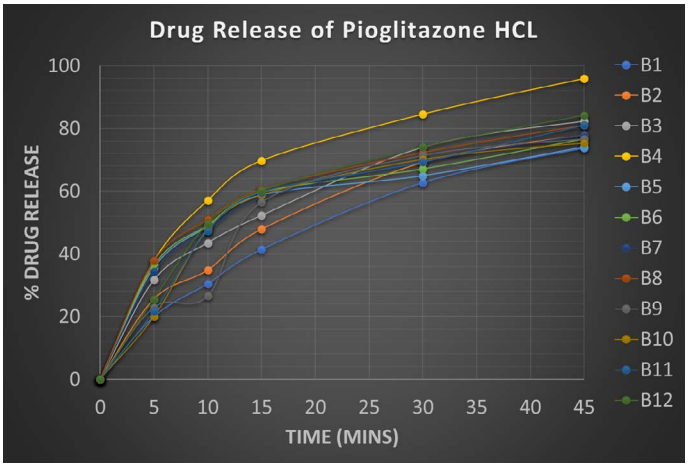


**Figure no 8:** Drug Release Profile of Pioglitazone HCL (Batch 1-12).

## 4. Conclusion

A safe and stable sustain release tablet was successfully developed with desired quality attributes having site-specific targeting, and good drug release for the treatment of Diabetes mellitus. Synergistic combination of both drugs leads to a reduction in dose. All the pre-compression parameters of all the batches were evaluated such as angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. The post- compression parameters such as thickness, hardness, friability, weight variation, disintegration time, drug content, and in-vitro dissolution studies were performed.

Thus, the result of the current study indicated that the Pioglitazone HCL and Caffeine matrix tablet under present investigation has a promising potential as a dosage form and can be used as an alternative to the available marketed conventional dosage form as it released an initial loading dose that can be useful for immediate release and maintenance dose can be useful for prolong or sustained release for better therapeutic benefits to control diabetes mellitus. Also, the formulation was found to be stable for a period of one month and the further stability studies are in progress.

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