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# DESIGN, DEVELOPMENT AND IN-VITRO EVALUATION OF SUSTAINED RELEASE TABLETS OF CALCIUM DOBESILATE

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**Abstract:**

Floating drug delivery systems are the gastroretentive forms that precisely control the release rate of target drug to a specific site which facilitate an enormous impact on health care. The purpose of this research was to develop a novel gastro retentive drug delivery system based on direct compression method for sustained delivery of active agent to improve the bioavailability, reduce the number of doses and to increase patient compliance. Gastro retentive floating tablets of Calcium dobesilate were prepared by direct compression method using altered concentrations of HPMC K4, HPMC K15 and PVP K30 as polymers. The prepared tablets of PRE were evaluated for hardness, thickness, friability, weight variation, drug content uniformity, buoyancy lag time, total floating time, in-vitro dissolution study, etc. The values of tablets average weight ranging from 642±9 to 659±7 mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5 % of the weight. The % drug content of all the formulated tablets were found within the limit. % drug content value of drug was within 98.56±0.14% to 99.85±0.47%. The results within the range indicate uniform of mixing. The maximum drug content was found in formulation F8. Prepared optimized formulation (F8) showed the release of drug form gastroretentive formulation 99.45% after 12 hrs. and marketed formulation showed the release of 98.78% after 2 hrs table 3 & 4. When the regression coefficient values of were compared [14-15], it was observed that 'R2' values of zero order was maximum i.e. 0.924 hence indicating drug release from formulations was found to follow zero order kinetics.

**Keywords**: Calcium dobesilate, floating tablet, gastro retentive, total floating time

## 1. Introduction

The oral bioavailability of many drugs is limited by their unfavourable physicochemical characteristics or absorption in well-defined part of the gastrointestinal tract (GIT) referred as "absorption window" [1]. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves the solubility for drugs that are less soluble in a high pH environment [2]. Various approaches have been investigated to increase the retention of oral dosage form in the stomach, including floating systems, swelling and expanding systems, bioadhesive systems, modified shape systems, high density systems, and other delayed gastric emptying devices [1]. Calcium dobesilate (calcium 2, 5- dihydroxybenzenesulfonate) is a drug used for the treatment of diabetic retinopathy and chronic venous insufficiency. Calcium dobesilate shows anti-platelet and fibrinolytic activities by inhibiting platelet activation factor (PAF) and enhancing the release of tissue plasminogen activator (tPA) and acts selectively on the capillary walls regulating their physiological functions of resistance and permeability [1-3]. The objective of the present research work was to provide gastroretentive formulation that will provide once daily, sustained release dosage form of Calcium dobesilate.

## 2. Materials and methods

### 2.1 Materials

Calcium Dobesilate was received as a gift sample from Pharmaceutical company. Hydroxypropyl methylcellulose (HPMC K4M, HPMC K15M) was procured from Meditab Specialities Pvt. Ltd., Satara. PVP K30 was purchased from S.D fine chemicals, Mumbai. Sodium bicarbonate, citric acid, magnesium stearate, talc were purchased from Mapromax, Life sciences Pvt. Ltd., Dehradun. Other solvents and chemicals used in the research were of LR grade. All the studies were carried in distilled water.

### 2.2 Methods

#### 2.2.1 Preparation and characterization of Calcium Dobesilate of floating tablet

Direct compression was followed to manufacture the gas generating floating tablets of Calcium Dobesilate. Nine different formulations (F1, F2, F3, F4, F5, F6, F7, F8, & F9) were prepared by direct compression [6]. All the polymers selected, drug and excipients were passed through sieve no. 40 before using into formulation. The amount and ratio of drug and polymers were weighed as per given in table no.1 and all the formulation were used for further evaluations parameters.

**Table 1: Various formulations of Calcium Dobesilate gastroretentive tablets**

| Excipients(mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **Calcium Dobesilate** | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |
| **HPMC K 5** | 50 | 75 | 100 | - | - | - | 25 | 37.5 | 50 |
| **HPMC K 16** | - | - | - | 50 | 75 | 100 | 25 | 37.5 | 50 |
| **PVP K30** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Citric acid** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **$NaHCO_3$** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **$Mg(C_{18}H_{35}O_2)_2$** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Talc** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Lactose** | 60 | 35 | 10 | 60 | 35 | 10 | 60 | 35 | 10 |
| **Total Weight** | 650 | 650 | 650 | 650 | 650 | 650 | 650 | 650 | 650 |

### 2.3 Determination of Bulk properties

#### 2.3.1 Bulk density

Bulk density is determined by measuring the volume of a known mass of powder sample that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup.

**Procedure :** Accurately weighed 1gm of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit. Calculate the bulk density in gm per ml, gm/cc by the formula.

**Bulk density = Bulk Mass/ Bulk Volume**

#### 2.3.2 Tapped density

Tapped density is determined by measuring the volume of a known mass of powder sample before and after the tapping that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup [7].

**Procedure :** Accurately weighed 10 gm of powder was poured into the measuring cylinder carefully level the powder and read the tapped volume (after 50-60 times tapping), $V_t$ to the nearest graduated unit. Calculate the tapped density in gm per ml, gm/ $cm^3$ by the formula:

Tapped density = Bulk Mass/ Tapped Volume

**2.3.3 Compressibility index (Carr's index):**

Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material [8].

It can be calculated as per given formula:

$$C.I. = \frac{\text{Tapped density- Bulk density}}{\text{Tapped density}} \times 100$$

**2.3.4 Hausner ratio**

It indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausner ratio = Tapped density / Bulk Density

**2.4 Evaluation of tablets**

All the tablets were evaluated for following different parameters which includes;

**2.4.1Thickness and diameter**

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used and an average value was calculated [9].

**2.4.2 Drug content**

Twenty tablets were taken and amount of drug present in each tablet was determined [66].The tablets were crushed in a mortar and the powder equivalent to 100 mg of drug was transferred to 100 ml standard flask. The powder was dissolved in 50 ml of 0.1 N HCl and made up to volume with of 0.1 N HCl. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at $\lambda_{max}$ of 316 nm using of 0.1 N HCl as blank.

**2.4.3 Hardness**

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

### 2.4.4 Friability

The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated [10].

$$\% \text{ Friability} = \frac{W1 - W2}{W1} \times 100$$

Where,

W1 = Initial weight of tablet before test

W2 = final weight of tablet after test

### 2.4.5 Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated [11].

### 2.4.6 *In vitro* buoyancy studies

*In vitro* buoyancy was determined by floating lag time as per the method [12]. The tablets were placed separately in a 100 ml glass beaker containing simulated gastric fluid (SGF), pH 1.2 as per USP. The time required for the tablet to rise to the surface and float was determined as floating lag time.

### 2.4.7 *In vitro* dissolution rate studies

*In vitro* drug release of the sample was carried out using USP- type II dissolution apparatus (Paddle type) [13]. The dissolution medium, 900 ml 0.1N HCl was placed into the dissolution flask maintaining the temperature of 37±0.50ºC and at 75 rpm. One Calcium Dobesilate tablet was placed in each basket of dissolution apparatus. The apparatus was allowed to run for 12 hours. Sample measuring 5 ml were withdrawn after every 1 hour up to 12 hours using 10 ml pipette. The fresh dissolution medium (37°C) was replaced every time with the same quantity of the sample and take the absorbance at 316 nm using spectroscopy.

## 3. Results and discussion

Direct compression was followed to manufacture the gas generating floating tablets of Calcium Dobesilate. And powder bland was evaluated for pre compression parameters. The

loose bulk density (LBD) and Tapped bulk density (TBD) of the powders of different formulations were evaluated before the compression of powders in to tablets. The bulk density and the tapped density for all the formulations varied from 0.423 to 0.438 gm/cm$^3$ and 0.536 to 0.545 gm/cm$^3$ respectively. The values obtained lies within the acceptable range. The difference exists between the bulk density and tapped density found to be very few. This result helps in calculating the % compressibility of the powder. The result of Hausner's ratio of all formulations ranges from 1.237 to 1267. Results of Hausner's ratio of all formulations were indicates that the flow ability of all the formulation. The results of the compressibility index of all the formulations ranges from 19.188% to 21.082%. Results clearly showed that the flow ability of all the formulations was good and also the powder had good compressibility table 2.

The thickness of the tablets was reported in the micrometer (mm).The thickness of tablet indicates that, die fill was uniform. The thickness depends on the size of the punches (8 mm) and the weight of one tablet (650mg). The value of thickness ranges between 4.2±0.2 to 4.5±0.2 mm. Friability determines the strength of the tablets. The friability for all the formulations was below 1% indicating that the friability was within the prescribed limits. The results of friability test indicate that the tablet possesses good mechanical strength. The friability value ranges from 0.478±0.065 to 0.852±0.041. The mean hardness values were measured for all the formulation using Monsanto hardness tester. The hardness value ranges from 6.2±0.2 to 6.5±0.1 kg/cm$^2$. Twenty tablets were randomly selected from each formulation and evaluated. The average weight of each formulation was recorded. The obtained data were almost uniform. The values of tablets average weight ranging from 642±9 to 659±7 mg. All the tablets passed weight variation test as the % weight variation was within the USP Pharmacopoeia's limits of ±5 % of the weight. The % drug content of all the formulated tablets were found within the limit. % drug content value of drug was within 98.56±0.14% to 99.85±0.47%. The results within the range indicate uniform of mixing. The maximum drug content was found in formulation F8 table 3.

Prepared optimized formulation (F8) showed the release of drug form gastroretentive formulation 99.45% after 12 hrs. and marketed formulation showed the release of 98.78% after 2 hrs table 4 & 5. When the regression coefficient values of were compared [14-15], it was observed that '$R^2$' values of zero order was maximum i.e. 0.924 hence indicating drug release from formulations was found to follow zero order kinetics table 6.

**Table 2: Result of pre-compression properties of blend**

| Formulation Code | Bulk density(gm/ml) | Tapped density(gm/ml) | Compressibility index | Hausner ratio |
|---|---|---|---|---|
| F1 | 0.423 | 0.536 | 21.082 | 1.267 |
| F2 | 0.432 | 0.545 | 20.734 | 1.262 |
| F3 | 0.425 | 0.536 | 20.709 | 1.261 |
| F4 | 0.431 | 0.536 | 19.590 | 1.244 |
| F5 | 0.435 | 0.542 | 19.742 | 1.246 |
| F6 | 0.436 | 0.544 | 19.853 | 1.248 |
| F7 | 0.431 | 0.542 | 20.480 | 1.258 |
| F8 | 0.435 | 0.542 | 19.742 | 1.246 |
| F9 | 0.438 | 0.542 | 19.188 | 1.237 |

**Table 3: Results of post compression properties of Calcium Dobesilate FGR tablets**

| Formulation code | Thickness* (mm) | Hardness* (kg/cm$^2$) | Weight variation* (mg) | Friability* (%) | Drug content* (%) | Total floating duration* (h) | Floating lag times* (sec) |
|---|---|---|---|---|---|---|---|
| F1 | 4.2±0.2 | 6.2±0.2 | 650±5 | 0.754±0.002 | 98.89±0.23 | 10±1.0 | 45±2 |
| F2 | 4.3±0.1 | 6.5±0.1 | 655±4 | 0.780±0.045 | 98.56±0.14 | 10±1.0 | 42±1 |
| F3 | 4.2±0.3 | 6.4±0.2 | 648±6 | 0.658±0.032 | 98.78±0.25 | 11±1.0 | 49±3 |
| F4 | 4.3±0.1 | 6.5±0.3 | 652±5 | 0.478±0.065 | 99.12±0.32 | 10±0.5 | 53±4 |
| F5 | 4.2±0.4 | 6.4±0.2 | 659±7 | 0.698±0.074 | 98.69±0.25 | 11±1.0 | 56±2 |
| F6 | 4.5±0.2 | 6.5±0.1 | 647±4 | 0.745±0.065 | 98.98±0.26 | 12±0.2 | 58±5 |
| F7 | 4.3±0.3 | 6.4±0.1 | 642±9 | 0.625±0.045 | 98.95±0.54 | 12±1.0 | 41±4 |
| F8 | 4.4±0.4 | 6.4±0.1 | 643±3 | 0.775±0.62 | 99.85±0.47 | 12±0.2 | 38±2 |
| F9 | 4.4±0.5 | 6.5±0.1 | 648±4 | 0.852±0.041 | 98.74±0.58 | 12±0.5 | 46±1 |

***Average of three determinations (n=3)**

**Table 4: *In-vitro* drug release study of GRF tablets**

| Time | % Cumulative Drug Release | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| (hr) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | M.F |
| 0.5 | 48.89 | 45.65 | 42.25 | 45.65 | 42.25 | 40.65 | 22.45 | 20.23 | 18.89 | 43.25 |
| 1 | 73.32 | 68.89 | 65.58 | 68.89 | 65.58 | 56.65 | 28.98 | 26.65 | 22.32 | 69.98 |
| 1.5 | 90.23 | 89.98 | 85.65 | 89.98 | 85.65 | 72.23 | 36.69 | 33.32 | 32.45 | 88.85 |
| 2 | 96.96 | 95.56 | 93.32 | 95.56 | 93.32 | 83.34 | 45.65 | 42.23 | 39.98 | 98.78 |
| 3 | 99.23 | 99.12 | 98.98 | 99.12 | 98.98 | 91.15 | 55.52 | 53.35 | 43.32 | - |
| 4 | - | - | - | - | - | 99.45 | 69.98 | 65.58 | 56.65 | - |
| 6 | - | - | - | - | - | - | 75.12 | 71.12 | 62.25 | - |
| 8 | - | - | - | - | - | - | 88.65 | 85.56 | 73.32 | - |
| 12 | - | - | - | - | - | - | 91.45 | 99.45 | 80.45 | - |

**M.F-marketed Formulation**

**Table 5: *In-vitro* drug release data for optimized formulation F8**

| Time (h) | Square Root of Time(h)$^{1/2}$ | Log Time | Cumulative*% Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|---|---|---|---|---|---|---|
| 0.5 | 0.707 | -0.301 | 20.23 | 1.409 | 74.35 | 1.871 |
| 1 | 1 | 0 | 26.65 | 1.602 | 60.02 | 1.778 |
| 1.5 | 1.225 | 0.176 | 33.32 | 1.659 | 54.42 | 1.736 |
| 2 | 1.414 | 0.301 | 42.23 | 1.745 | 44.38 | 1.647 |
| 3 | 1.732 | 0.477 | 53.35 | 1.800 | 36.88 | 1.567 |
| 4 | 2 | 0.602 | 65.58 | 1.885 | 23.35 | 1.368 |
| 6 | 2.449 | 0.778 | 71.12 | 1.949 | 11.02 | 1.042 |
| 8 | 2.828 | 0.903 | 85.56 | 1.971 | 6.55 | 0.816 |
| 12 | 3.464 | 1.079 | 99.45 | 1.999 | 0.22 | -0.658 |

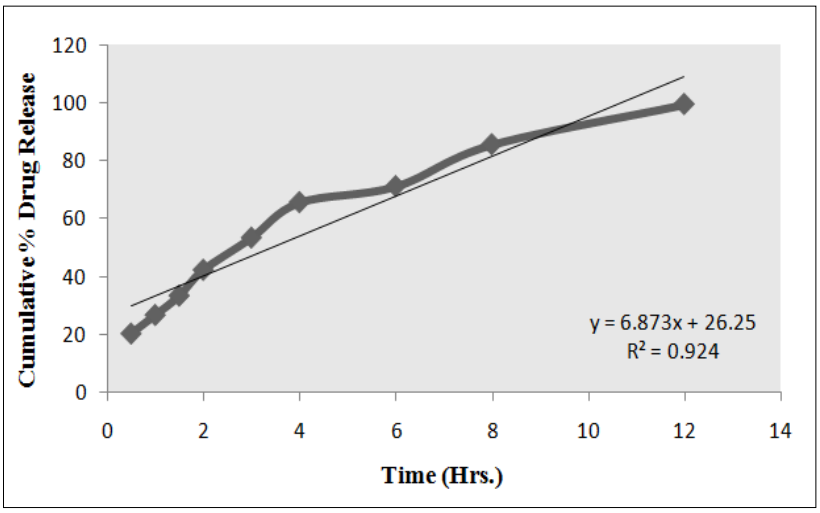


**Figure 1: Cumulative % drug released Vs Time**

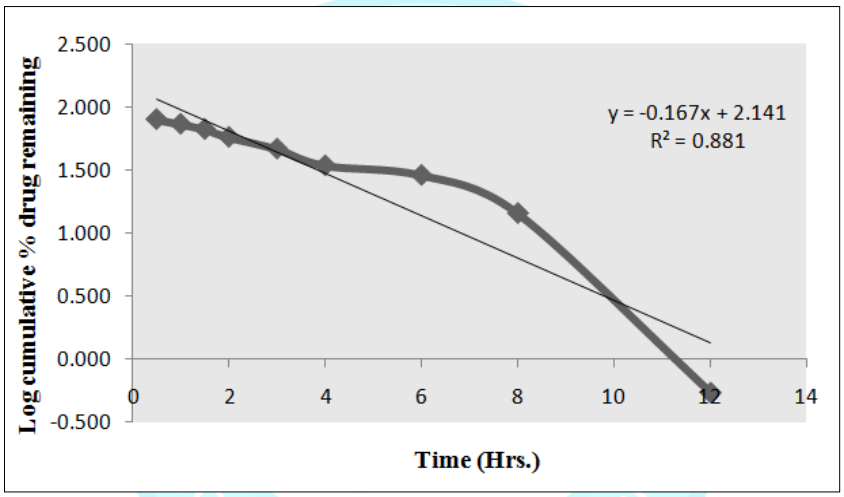


**Figure 2: Log cumulative % drug remaining Vs Time**

**Table 6: Regression analysis data of Calcium Dobesilate floating tablets**

| Batch | Zero Order | First Order |
|---|---|---|
| | $R^2$ | |
| **F8** | 0.924 | 0.881 |

## 4. Conclusion

Hydrodynamically balanced systems of Calcium Dobesilate with shorter lag time can be prepared by direct compression method using HPMC and $NaHCO_3$ as gas generating agent. All the prepared tablet formulations were found to be good without capping and chipping. As the amount of polymer in the tablet formulation increases, the drug release rate decreases.

Most of the designed formulations of Calcium Dobesilate displayed zero order release kinetics and drug release follows zero order kinetic model.

## 5. Acknowledgements

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## 6. Conflict of Interest

The authors declare that there is no conflict of interest.

## 7. References

1. S. Shahi, A. Sonawane, S. Vanamore, and N. Zadbuke, "Formulation and in-vitro characterization of acyclovir floating matrix tablets: a factorial design study," Journal of Applied Pharmaceutical Science, vol. 3, no. 5, p. 65, 2013.
2. A. Yadav and D. Jain, "Formulation development and characterization of gastroretentive floating beads," Asian Journal of Pharmacy and Medical Science, vol. 2, no. 1, pp. 1–10, 2012.
3. Angehrn F. Efficacy and safety of calcium dobesilate in patients with chronic venous insufficiency: an open-label, multicenter study, Current Therapeutic Research 1995; 56(4): 346-357.
4. Casley smith JR. A double-blind trial of calcium dobesilate in chronic venous insufficiency, Angiology 1988; 39(10):853-857.
5. Barras JP, Effect of calcium dobesilate on blood viscosity in diabetic microangiopathy. A review, Michal M. Vasa 1986; 15(3):200-205.
6. D. Saritha, D. Sathish and Y. Madhusudan Rao. Formulation and Evaluation of Gastroretentive Floating Tablets of Domperidone Maleate. Journal of Applied Pharmaceutical Science 2(3); 2012:68-73.
7. Newman AW. Micromeritics: Brittain HG; Physical Characterization of Pharmaceutical Solids. Marcel Dekker Inc, Newyork; Basel, 1995; 70; 293-294.
8. Newman AW. Micromeritics: Brittain HG; Physical Characterization of Pharmaceutical Solids. Marcel Dekker Inc, Newyork; Basel, 1995; 70; 271-275.
9. Wells J; Pharmaceutical Preformulation: Aulton ME; Pharmaceutics: The Science of dosage form design. 3 rd edi, Edinburg, London, Melbourne, Newyork, 1998; 247.
10. Ajay B., Dinesh KP, Pradeep S. Studies on formulation and evaluation of floating tablets of ciprofloxacin. Int J ComprenPharma. 2010; 5(2); 1-3.

11. Prakash RB, Neelima AK, Snehith VS, Ramesh C. Development of gastro retentive drug delivery system of cephalexin by using factorial design. ARS Pharma. 2009; 50(1); 8-24.
12. Rosa M, Zia H, Rhodes T. Design and testing in vitro of a bioadhesive and floating drug delivery system for oral application. Int J Pharm. 1994; 105(1); 65-70.
13. Shailesh P, Laxmanbhai P, Chhaganbhai P. Floating matrix tablets of domperidone formulation and optimization using simplex lattice design. Indian J Pharm Res. 2011; 10(3); 447-55.
14. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci 1963; 52:1145-49.
15. Korsmeyer, R.W.; Gunny, R.; Peppas, N.A. Mechanism of solute release from hydrophilic polymers.Int. J. Pharm., Amsterdam, v.15, p.25-35, 1983.