Formulation and Evaluation of Calcium Acetate Tablet

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Abstract: The present study was designed to investigate the suitable diluents and to develop a robust formulation of Calcium acetate tablet. For comparative study six different formulations (F-1 to F-6) of Calcium acetate were designed and tablets were manufactured by wet granulation manufacturing method. The granules were evaluated for angle of repose, loose bulk density, tapped bulk density, compressibility index, Hausner ratio, Angle of repose and drug content. Then the prepared tablets were evaluated in terms of their physical parameters including weight variation, hardness, friability, thickness and disintegration time. *In vitro* release studies were performed using USP type II apparatus (paddle method) in 900 mL of Purified water at 50 rpm for 30 minutes and finally assay carried out for evaluation and characterization of these formulations. The tablets of formulation F-1 showed better performance as compared to others in terms of dissolution and other physical parameters and our result suggests that Calcium acetate should be formulated by using maize starch as diluent to remove processing complexities.

Key words: Calcium Acetate · Wet Granulation · Hyperphosphatemia · Kidney Failure

INTRODUCTION

Calcium acetate is a chemical compound which is calcium salt of acetic acid. It has the formula $Ca(C_2H_3O_2)_2$. Its standard name is calcium acetate, while calcium ethanoate is the systematic name. An older name is acetate of lime. The anhydrous form is very hygroscopic; therefore the monohydrate $(Ca(CH_3COO)_2 \cdot H_2O)$ is the common form.

Calcium is a mineral that is needed for many functions of the body, especially bone formation and maintenance. Calcium can also bind to other minerals such as phosphate and aid in their removal from the body. Hyperphosphatemia, a common complication in patients with end-stage renal disease, is treated with oral phosphate binding medications that restrict phosphorus absorption from the gastrointestinal tract [1]. Now a days Calcium containing phosphate binders are used increasingly, instead of aluminum hydroxide [2]. Some reports have shown that calcium acetate binds phosphorous more effectively than calcium carbonate; therefore, it has many characteristics of an ideal phosphate binder. It is, for instance, a more readily soluble salt compared to calcium carbonate [3-6]. Calcium acetate is used to control phosphate levels to keep them from getting too high in people with kidney failure.

The oral route of drug administration is the most important method of administering drugs for systemic effects [7]. Oral dosage forms are intended for systemic effects resulting from drug absorption through gastro intestinal tract. The most common solid dosage forms in contemporary practice are tablets. In the present study, we prepared six new formulations of calcium acetate tablet and evaluated its *In vitro* characteristics including disintegration time and dissolution rate.

MATERIALS AND METHODS

For this present investigation Calcium Acetate was procured from VASA PHARMACHEM PVT. LTD. Microcrystalline cellulose PH101, Crospovidone (Kollidon CL), Polyethylene Glycol 6000 (Macrogol 6000), Maize Starch and Lactose were procured from Local commercial source. Magnesium Stearate, was procured from Remo Chemicals Dhaka.

All other ingredients used throughout the study were of analytical grade and were used as received. The experiments were carried out in 2012.

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Table 1: Composition of different formulations of Calcium Acetate 667 mg tablet.

Ingredients (mg/Tab.)	Formulations					
	F-1	F-2	F-3	F-4	F-5	F-6
Calcium Acetate	717.2	717.2	717.2	717.2	717.2	717.2
Crospovidone (Kollidon CL)	37	37	37	37	37	37
Polyethylene Glycol 6000 (Macrogol 6000)	21.5	21.5	21.5	21.5	21.5	21.5
Maize Starch	108	-	-	54	54	-
Lactose	-	108	-	54	-	54
Microcrystalline Cellulose (PH 101)	-	-	108	-	54	54
Maize Starch as paste	33.3	33.3	33.3	33.3	33.3	33.3
Magnesium Stearate	8	8	8	8	8	8
Purified Water	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.
Total	925	925	925	925	925	925

Preparation of Calcium Acetate Tablets: Maize starch, Lactose, Microcrystalline Cellulose (PH 101); (whichever is applicable), Calcium Acetate and 85% Crospovidone (Kollidon CL) were sieved separately through sieve no. 24 and mixed thoroughly. Solution of Polyethylene Glycol 6000 (Macrogol 6000) and Starch paste were prepared of remaining portion of Maize Starch with purified water and added to the powder blend. The wet mass was dried in fluid bed dryer at 65±5°C and sized through 2 mm screen. Remaining portion of Crospovidone (Kollidon CL), Aerosil 200 and Magnesium Stearate was sieved through mesh # 40 and added to the granules. The tablets were compressed in Pilot Press Compression Machine (India) using 19 x 9 mm standard concave oval shaped punch.

Evaluation of Granules: Before final compression of tablets, granules was subjected to precompression parameters such as bulk density, tapped density, angle of repose, powder compressibility and Hausner ratio. All the experiments were done in triplicates and expressed as mean ± SD.

Bulk Density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of granules lightly shaken to break any agglomerates formed was introduced into a 10 ml measuring cylinder. After the initial volume observed, the cylinder was allowed to fall under its own height onto hard surface from the height of 2.5 cm at 2 seconds interval. The tapping was continued until no further change in the volume was noted. (LBD) and (TBD) were calculated by using the following formulas [8].

- LBD = Weight of the powder / volume of the packing
- TBD = Weight of the powder /tapped volume of the packing

The Compressibility Index: The compressibility index of the granules was determined by carr's compressibility index [9].

$$\text{Carr's index (\%)} = [(TBD - LBD) \times 100]/TBD$$

Hausner's Ratio: Hausner found that the ratio D_F/D_o was related to inter particle friction and as such, could be used to predict powder flow properties.

- Hausner's factor = Tapped bulk density/Loose bulk density

Angle of Repose: Static angle of repose of the granules were determined by the funnel method. The accurately weighed granules were taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation [10].

$$\text{Tan} = h/r$$

Where "h" and "r" are the height and radius of the powder cone.

Evaluation of Calcium Acetate Tablets
Weight Variation Test: To study weight variation, 20 tablets from each formulation were weighed using an electronic balance and the test was performed according to the official method.

Hardness: For each formulation, the hardness of 6 tablets was determined using the PHARMA TEST Hardness Tester Machine.

Thickness: The thicknesses of the tablets were determined by using a digital slide calipers. Five tablets from each batch were used and average values were calculated.

Friability: Friability of 20 tablets of each proposed formulations were determined using the PHARMA TEST Friability Tester.

***In vitro* Disintegration Time:** The *In vitro* disintegration time was determined using disintegration test apparatus (Eureka Alpha/Numeric Disintegration tester) according to pharmacopoeial method in water. A tablet was placed in each of the six tubes of the apparatus and a disc was added to each tube. The time was taken for complete disintegration of the tablet with no discernible mass remaining in the apparatus was measured.

***In vitro* Dissolution Test:** The *In vitro* dissolution studied was carried out using USP 24 dissolution apparatus type II (USP 24) (paddle method) at 50 rpm. Dissolution test was carried out for a total period of 30 minutes using 900 ml Purified water as dissolution medium at $37 \pm 0.5°C$. The samples were filtered through 0.45ì membrane filter and drug content in each sample was analyzed after suitable dilution by titration with 0.05M Disodium edetate using Calconcarboxylic acid Triturate as indicator.

Drug Content: Five tablets were weighed individually and the drug was extracted in Purified water. The solution was filtered through 0.45 µ membrane filter paper. Then drug content in each sample was analyzed by titration with 0.05M Disodium edetate using Calconcarboxylic acid Triturate as indicator.

RESULTS AND DISCUSSION

Characterization of Granules: The granules of the different proposed formulations was evaluated for LBD, TBD, Compressibility index, Hausner ration and angle of repose (Table. 2). The results of LBD and TBD ranged from 0.512 ± 0.01 to 0.638 ± 0.016 and 0.662 ± 0.017 to 0.794 ± 0.013 respectively. The results of compressibility index (%) ranged from 18.68 ± 1.05 to 22.66 ± 0.84. Generally compressibility index values 12 to 21 result in good to fair flow properties. The results of Hausner ratio ranged from 1.23 ± 0.03 to 1.292 ± 0.04. Hausner ratio values less than

Table 2: Comparison of bulk density, Compressibility Index, Hausner ratio and Angle of Repose of granules of different formulations

Formulation	Loose Bulk Density (LBD)(gm/ml)	Tapped Bulk Density (TBD) (gm/ml)	Compressibility Index (%)	Hausner ratio	Angle of Repose (°)
F-1	0.592±0.02	0.728±0.012	18.68±1.05	1.23±0.03	27.28±0.52
F-2	0.638±0.016	0.794±0.013	19.65±0.53	1.245±0.04	29.64±1.21
F-3	0.512±0.01	0.662±0.017	22.66±0.84	1.292±0.04	27.15±1.00
F-4	0.621±0.016	0.779±0.010	20.28±0.83	1.255±0.07	29.64±1.01
F-5	0.601±0.011	0.760±0.005	20.92±0.54	1.265±0.05	30.52±0.15
F-6	0.611±0.016	0.764±0.010	20.03±0.83	1.251±0.07	29.04±0.78

Table 3: Physicochemical properties of Calcium acetate tablets of different formulations

Formulation	Average weight (mg) ± SD (n = 20)	Diameter (mm)	Thickness (mm) ± SD (n = 5)	Hardness (Kp) ± SD (n = 6)	Friability (%) (n = 20)	Disintegration time (Sec)	Drug Content (%) ± SD (n = 5)
F-1	925.59±1.05	19x9	6.12±0.03	10.12±0.45	0.45	8 to 9 min	100.14±1.10
F-2	924.86±0.935	19x9	6.05±0.10	9.05±0.71	0.88	10 to 13.5 min	99.86±0.87
F-3	925.36±1.001	19x9	6.22±0.08	9.98±1.02	0.66	12 min to 14 min	100.01±1.33
F-4	926.30±0.652	19x9	6.03±0.038	9.90±0.504	0.54	9 to 12.5 min	99.84±0.82
F-5	924.42±0.582	19x9	6.11±0.058	9.87±0.74	0.56	10.5 to 14 min	100.05±1.43
F-6	926.12±0.759	19x9	6.14±0.13	10.25±0.65	0.75	11 to 13.5 min	100.84±0.78

Table 4: Comparison of *In vitro* release profile of Calcium Acetate tablet of different formulations.

Formulation	Release after 15 minutes (%)	Release after 30 minutes (%)	Release after 45 minutes (%)
F-1	65.30	94.53	100.24
F-2	54.05	83.46	92.10
F-3	49.91	74.88	88.63
F-4	59.35	81.25	95.06
F-5	41.60	76.58	85.75
F-6	46.36	78.92	90.47

1.25 results in good flow properties. So the granules of almost all formulations showed good flow properties. The result of angle of repose ($\leq30°$) indicates good flow

properties of powders which was supported from the results found from compressibility index. All these results indicate that the granules possessed satisfactory flow properties and compressibility.

Physicochemical Evaluation of Calcium Acetate Tablets: The tablets were evaluated in terms of physical parameters (weight variation, hardness, thickness and friability) disintegration time and drug content (Table 3). The thickness of the tablets were found between 6.03 ± 0.038 mm to 6.22 ± 0.08 mm, hardness of the tablets ranged from 9.05 ± 0.71 kg/cm^2 to 10.25 ± 0.65 kg/cm^2 and friability ranged from 0.45% to 0.88%. The weight
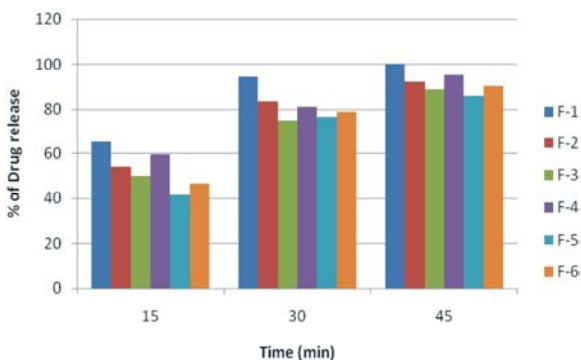
Fig1: Drug release profile of different formulations at different time intervals

variations of prepared tablets complied with the pharmacopoeial specifications. The disintegration times were found between 8 to 14 minutes. The release profile of different formulations of Calcium acetate tablets are shown in Figure. 1.

As per the dissolution study tablets of different formulations showed 100.24%, 92.10%, 88.63%, 95.06%, 85.75% and 90.47% drug release in 45 minutes respectively (Table. 4). Although tablets from all different formulations released almost similar amount of drug at the end of 45 minutes and passed Pharmacopoeial specification formulation F-1 released highest amount of drug. Tablets of formulation F-1 showed better dissolution performance throughout the time which is more acceptable.

CONCLUSION

The results found in different tests of Calcium acetate tablets of different formulations show that maize starch, lactose and microcrystalline cellulose (PH 101) can be used as diluents but tablet of the formulation containing maize starch shows better dissolution performance. Another advantage is that maize starch is slightly cheaper in comparison to lactose and microcrystalline cellulose (PH 101). Therefore in the light of observed data we can conclude that maize starch is more suitable as diluents to prepare a cost-effective quality product and robust formulation of Calcium acetate tablet.

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