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Development and Evaluation of Chewable Tablets of Calcium and Vitamin D

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ABSTRACT

The aim of research work was to prepare a formulation of calcium and vitamin D chewable tablets by wet granulation method using excipients and to evaluate the tablet properties. In this research work vitamin D3 was used as vitamin D. The blend was compressed on a rotary compresson machine. Tablets were subjected to various tests (weight variation, thickness, hardness and assay of calcium and vitamin D3 etc) and the results were in compliance with the pharmacopoeial specifications. All physical properties studied indicate that all excipients are good pharmaceutical excipients for tablets. The aim of this work was to minimise the complexity of formulation and to make cost effective product. Since tablets to be prepared are chewable so sweetening and flavouring agents are to be incorporated to make the tablet palatable and easily acceptable.

Keyboards: Calcium, vitamin D3, wet granulation, chewable tablet, tablet formulation.

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INTRODUCTION

Vitamin D refers to vitamin D2 (Ergocalciferol) or vitamin D3 (Cholecalciferol). In the present research work vitamin D3 was used as vitamin D. Vitamin D improves bone health and deficiency causes painful bone disease known as osteomalacia.

Deficiency of vitamin D also causes muscle weakness and fractures [1]. There is a relationship between the intakes of calcium either alone, or in combination with vitamin D, and reducing the loss of bone mineral density (BMD). Reduction in the risk of bone fractures are related to the reducing the loss of BMD. Calcium and vitamin D may also reduce the loss of bone mineral in post-menopausal women [2].

Incidence of osteoporotic bone fractures can be changed by the combination of calcium and vitamin D. The combination of calcium and vitamin D can be effective in the prevention and treatment of steroid- induced osteoporosis in adults (older than 18 years) [3,4,5,6].

PREFORMULATION STUDY [7, 8]

Preformulation studies are the first step in the development of dosage form of any drug substance. The objective of preformulation studies are to develop a portfolio of information about the drug substance, so that this information is useful to develop formulation. Preformulation investigations are designed to identify those physicochemical properties and excipients that may influence the formulation design, method of manufacture and pharmacokinetic-bio pharmaceutical properties of the resulting product. Preformulation studies includes- description of the substance, taste, odour, colour, loss on drying, bulk density, tapped density, carr's index, hausner's ratio, angle of repose, incompatibility with other ingredients etc.

MATERIALS AND METHODS

Materials that are used for formulation are tricalcium phosphate, mannitol-25, sucrose, PVPK-30, vitamin D3, aspartame, aerosil, strawberry flavour powder, talc and magnesium stearate. All materials were received as gift samples from a pharmaceuticals manufacturing company.

Table: 1 Formulation table

S. No.	Name of Material	Quantity Per Tablet (in mg)
1.	Tricalciam Phosphate	357.15
2.	Mannitol-25	100
3.	Sucrose	40.60
4.	PVPK-30	24
5.	Vitamin-D3 (100 IU/mg)	1
6.	Aspartame	30
7.	Aerosil	18
8.	Strawberry Flavour Powder	13.25
9.	Talc	8
10.	Magnesium Stearate	8
11.	D M Water	QS
	TOTAL	**600**

METHOD

Wet granulation method was used to prepare the granules for the tablets. Mass mixer was used to mix tricalcium phosphate, mannitol-25, and sucrose. These materials were passed through 40 mess size and mixed for 20 minutes. A solution of PVPK-30 was prepared by dissolving it in hot DM water with continuous stirring. The solution was added in the mass mixer and a damp mass was formed. The damp mass was dried at 70-75 C for 2 hours in tray dryer and then transferred into multi-mill to reduce the size. Finally the semi-dry granules were again dried in tray dryer at 70-75 C for 2 hours. Vitamin D3, aspartame, aerosol, strawberry powder flavor, talc and magnesium stearate were sieved through 40-mesh size and mixed thoroughly with dried granules in a blender. Powder blend sample was taken for evaluation studies. Tablets were compressed on a rotary compression machine. Sample of compressed tablets was taken for evaluation studies.

Evaluation of Chewable Compressed tablets

Tablets properties were evaluated by pharmacopoeial and non-pharmacopoeial tests.

Organoleptic properties of tablets:

Colour, taste and flavour of tablets was checked manually by seeing, chewing and smelling the tablets.

Weight variation test:

20 tablets were used to carry out the weight variation test. All tablets were weighed individually on a digital balance and average weight was calculated. Individual weights were compared with average weight.

Diameter and thickness test:

Micrometre screwguage was used to determine the diameter and thickness of each tablet. Random sample of 10 tablets was selected and their diameter and thickness were calculated in mm.

Hardness:

Hardness test was done to measure the crushing strength of tablets. Hardness of randomly selected 10 tablets was measured using hardness tester.

Friability:

Friability test apparatus was used to determine the friability of tablets. Friability was calculated after 100 rpm.

Assay:

Assay for Calcium: Titrimetric method [9]

Reagents:

Ammonia buffer pH 10.9: Prepared by dissolving 67.5 gm. of ammonium chloride in sufficient 10 M ammonia to produce 1000 ml.

Mordant black II triturate: Prepared by mixing 1 part of mordant black with 99 parts of sodium chloride.

Procedure:

20 tablets were crushed into fine powder. About 71 mg of tablet powder was taken in a conical flask with 5 ml dilute hydrochloric acid and 30 ml of water. Boiled the solution for 2 minutes; allowed for cooling and diluting up to 50 ml with water. 10 ml of ammonia buffer was added. Titration was done with 0.05M disodium edetate (Each ml of 0.05M disodium edetate is equivalent to 2.004 mg of elemental calcium) using mordant black II triturate as indicator until the colour change from pink to blue.

Content of elemental calcium per tablet was calculated by using following equation:

$$\frac{V \times F \times 2.004 \times W}{WT}$$

$$\frac{7.5 \times 0.986 \times 2.004 \times 600}{71.3 \text{ mg/tablet}}$$

$$= \quad 124.7 \text{ mg / tablet}$$

where

V= Volume of 0.05M disodium edetate used in ml (7.5 ml)

F=Factor of titre (0.986)

WT=Weight of sample taken in mg (71.3 mg)

W=Average weight of tablet in mg (600 mg)

Assay for Vitamin D3: HPLC Method [9]

Mobile Phase: Acetonitrile : Methanol= 91:09

Chromatographic system:

Flow rate: 1.5 ml/min.

Column: Octadecylsilyl silica gel for liquid chromatography (C18).(size: 4.6mm 250mm,5um)

Detector: 265nm, UV

Injection Volume: 20 µl

Temperature: 40 C

Procedure:

Standard Preparation: Accurately weigh 100 mg of Cholecalciferol was taken in 100 ml volumetric flask. 30 ml of methanol was added and then sonicated to dissolve. Volume up to 100 ml was completed by using methanol and mixed well. About 2 ml of this solution was diluted to 50 ml by using methanol.

Sample Preparation: 20 tablets were crushed into fine powder. 590 mg of fine powder was taken in a 50 ml volumetric flask. 30 ml of methanol was added and sonicated to dissolve. Volume up to 50 ml was completed with methanol.

Chromatographic Procedure: Before injection, filtration was done through 0.2 µ syringe filter. Separately 20 µl of prepared sample was injected in to the chromatograph. Chromatograms were recorded and measure the responses for major peaks. The content of cholecalciferol was calculated by using following equation:

$= \frac{AT}{AS} X \frac{WS}{100} X \frac{2}{50} X \frac{50}{WT} X \frac{Ps}{100} X W$ mg per tablet

= 28304/28455 x 99.0/100 x 1/50 x 50/590 x 100000/100 x 600 IU per tablet.

= 100.1 IU per tablet

where

AT=Area of sample preparation (28304)

AS=Area of standard preparation (28455)

WT=Weight of sample in mg (590 mg)

WS=Weight of standard cholecalciferol in mg (99 mg)

Ps=Potency of cholecalciferol standard (100000 IU/gm)

W=Average weight of tablet (600 mg)

RESULT AND DISCUSSION

Evaluation of powder blend was done before compression of tablets. Various parameters were calculated to determine the quality of granules which is responsible for good quality of tablets. Bulk density, tapped density, carr's index, hausner's ratio and angle of repose was calculated. These values are shown in the table below. All these values were found within the limits.

Evaluation result of powder blend :

Table: 2 Evaluation result of powder blend

S. No.	Parameters	Result
1.	Bulk Density (g/ml)	0.74
2.	Tapped Density (g/cc)	0.85
3.	Carr's Index (%)	11.76
4.	Hausner's Ratio	1.120
5.	Angle of Repose	30.58

Wet granulation method was used to prepare the calcium and vitamin D3 chewable tablets by using different types of excipients. Tablet properties were evaluated by performing various tests. In organoleptic tests - it was found that tablets are white coloured, sweet and strawberry flavoured. The result of weight variation test was +1.05% and -0.86%. Weight variation test is an indicator of variations in the drug content. The results of average diameter and thickness were 8.2mm and 3.3 mm respectively (within limits). Hardness of tablet was 6 kg (permissible limit is not less than 4 kg). Friability test indicates the mechanical strength of tablets. The result of friability test was also within specified limits of not more than 1.0%. The calcium content was assayed by titrimetric method and result was 124.5 mg/tablet (within limits). Vitamin D3 was determined by HPLC method and the result was 100.1 IU/tablet (within limits). All results are shown in the table.

Table: 3 Evaluations of Tablets

S. No.	Tests	Specifications	Result
1.	Average weight / Tablet	570 -630 mg	600
2.	Weight Variation	± 5 %	within limits
3.	Diameter	8.1 – 8.3 mm	8.2 mm
4.	Thickness	3.2 – 3.4 mm	3.3 mm
5.	Hardness	Not less than 4.0 kg	6.0 kg
6.	Friability	Not less than 1.0%	0.15%
7.	Assay: a) Content of Calcium per Tablet	112.5 -137.5 mg	124.7 mg
	b) Content of Vitamin D 3 per tablet	Not less than 90 IU	100.1 IU

CONCLUSION

In the present work calcium and vitamin D chewable tablets were manufactured successfully which fulfill all the required pharmacopoeial limits. This type of study is not only for this combination but also can be done on other drugs also. Present data can be used as a reference for future work.

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