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## Formulation of Vitamin D3 + Calcium tablets and evaluation of Physical and chemical Properties

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### ABSTRACT

The aim of this investigation was to develop Vitamin D3 and Calcium tablets by wet granulation method using excipients and to compare the tablet properties with BP specification. The blend was compressed on a single punch machine, tablets were subjected to various tests (weight variation, diameter and thickness, hardness, disintegration and assay of the drug) and the results were also in compliance with the official specifications. All the physical properties studied indicated that all excipients are good pharmaceutical excipients in tablets. The objective of this work was to present Vitamin D3 in granular and tablet form with improved dispersability, to minimize the complexity of formulations and to make cost effective product.

**Keywords:** Vitamin D3 and Calcium, tablet formulation, wet granulation.

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### INTRODUCTION

Vitamin D3(cholecalciferol) is derived from 7-dehydrocholesterol and involved in bone health. Scientists have recognized that, depression, back pain, cancer, both insulin resistance and pre-eclampsia during pregnancy, impaired immunity and macular degeneration are directly linked to the Vitamin D3 deficiency [1]. Inadequate Vitamin D3 may cause secondary hyperparathyroidism that increases the risk of osteoporosis and fractures and change the regulatory mechanisms of parathyroid hormone (PTH) [2]. Other types of condition such as high blood pressure, fibromyalgia, diabetes, multiple sclerosis, rheumatoid arthritis has been linked to the low levels of Vitamin D3 [3,4,5]. Vitamin D3 deficiency is responsible psychiatric and neurologic disorders and associated with low mood [6]. Vitamin D3 improves bone health and deficiency causes a painful bone disease known as osteomalacia. Deficiency of Vitamin D3 also causes exacerbates muscle weakness and turn to fractures [7]. 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 [8]. Bone mineral density (BMD) or 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) [9,10,11,12].

The objective of the present study is to develop a formulation of Calcium and Vitamin D3 tablet by wet granulation process and evaluation of its Physical and chemical properties.

### MATERIALS AND METHODS

**Materials:** Chemicals that were used for formulation are given in table 1. All chemicals were procured from commercial sources.

	<b>Chemicals</b>	<b>Amount (per tablet)</b>
1	Calcium Carbonate	1250 mg
2	Vitamin D3	2.00 mg
3	Maize Starch (as paste)	25 mg
4	Maize Starch( as dry mix)	25.00 mg
5	Lactose monohydrate	25.00 mg
6	Sodium Methyl paraben	1.00 mg
7	Sodium Propyl paraben	0.24 mg
8	Povidone K-30	16.00 mg
9	Purified talc	2.00 mg
10	Magnesium stearate	2.00 mg
11	Maize Starch dry	45.00 mg

#### **Preparation Method:**

Wet granulation method was used to prepare the tablets. Mass mixer was used to mix the Calcium Carbonate, Lactose monohydrate and Maize Starch. These materials were passed through 40-mesh size screen and mix for 20 minutes. Make a solution of Povidone K-30 in hot DM water. Stirring was continued until making a clear solution. Slurry was prepared by using Maize Starch, Sodium Methyl paraben and Sodium Propyl paraben. This slurry was added in clear solution of Povidone K-30. This mixture was called paste. Then paste was added in mass mixer and makes a wet mass which mixed for 10 minutes. Wet mass was dried in Fluid Bed Dryer (FBD) at 70-75°C for 30 minutes and then transfer into the multi mill to reduce the size. Finally it was again transferred to Fluid Bed Dryer (FBD) for final drying at 60-65°C for 10 minutes.

#### **Methods for Evaluation of Tablet Properties**

Tablets properties were evaluate by using BP and by non-pharmacopoeial tests.

#### **Weight variation test**

20 tablets were used to carry out the weight variation test. 20 tablets were weighed individually on an digital balance (Digital Balance, Model No. Ek 6001, Origin: Precisa, Switzerland) and calculate the average weight. Individual weight was compared with average weight.

#### **Length, Width and Thickness**

Micrometer screw gauge was used to determine the length, width and thickness of each tablet. Random samples of 10 tablets were selected and their length, width and thickness was calculated in mm.

#### **Hardness:**

Hardness test was done to measure the tablet crushing strength. Hardness of randomly selected 10 tablets was measured using Hardness Tester (Model No. HT-50, Origin: Thermonic, India).

#### **Friability:**

Friabilator (Friability Machine, Model No. 902, Origin: Electronic, India) was used to determine the Friability of tablets. This consists of a plastic chamber that revolves at 25 rpm. After operation tablets were reweighed.

#### **Disintegration Test**

Six tablets were putting in basket rack assembly (Disintegration Test Apparatus, Model No.: D-17, Origin: Electronic, India) to measure the Disintegration time. Six disks were used to avoid floating of tablets in 900 ml distill water maintained at 37±2°C.

**Assay:****Assay for calcium (Titrimetric Method)****Reagents:**

1. Ammonia buffer P<sup>H</sup> 10.9: Prepared by dissolving 67.5 g of ammonium chloride in sufficient 10 M ammonia to produce 1000 ml.

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

**Procedure:**

20 tablets were crushed into fine powder. About 88mg of tablet powder (About 88 mg of tablet powder is equivalent to about 30mg of calcium) was taken in a conical flask with 5ml dilute hydrochloric acid and 30ml of water. Boiled the solution for 2 minutes; allowed for cooling and diluting up to 50 ml with water. 10 ml of ammonia buffer (p<sup>H</sup> 10.9) was added. Titration was done with 0.05M disodium edentate (Each ml of 0.05M disodium edentate is equivalent to 2.004mg of elemental calcium or 5.004mg of calcium carbonate) using mordant black II triturate as indicator until the color change from pink to blue.

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

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

V=Volume of 0.05M disodium edentate required in ml.

F= factor of the titre.

WT= weight of sample taken in mg.

W=average weight of the tablet taken in mg.

**Assay For Vitamin D<sub>3</sub> (HPLC method):**

Mobile Phase: Acetonitrile : methanol = 91 : 09

Chromatographic system

Flow rate: 1.5ml/min

Column: Octadecylsilyl silica gel for liquid Chromatography (C<sub>18</sub>). (size: 4.6mm×250mm, 5µm).

Detector: 265nm, UV

Injection volume: 20µl

Temperature: 40<sup>0</sup> C

**Standard Preparation:** Accurately about 100mg of Cholecalciferol was taken in 100ml volumetric flask. 30ml of methanol was added and then sonication for proper dissolve. Volume up to 100 ml was completed by using methanol and mix well. About 2ml of this solution was diluted to 50 ml by using same diluent.

**Sample Preparation:** 20 tablets were crushed into fine powder. 1215 mg of those powder was taken into 50 ml volumetric flask. 30 ml of methanol was added and sonicated for dissolve. Finally volume up to 50ml was filled with same solvent methanol.

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

**Calculation:** Content of Cholecalciferol(IU)

$$\frac{AT}{AS} \times \frac{WS}{100} \times \frac{2}{50} \times \frac{50}{WT} \times \frac{Ps}{100} \times W \text{ mg/tablet}$$

=X IU of Cholecalciferol.

Where,

AT= Area of sample preparation.

AS= Area of standard preparation.

WT= Weight of sample in mg.

WS= Weight of Standard Cholecalciferol (vitamin D<sub>3</sub>) in mg.

Ps=Potency of vitamin D<sub>3</sub> standard.(100000 IU/gm)

W=Average weight of tablet.

100000 IU/gm

1mg=100 IU

2mg=200 IU =one tablet contain 200 IU vitamin D<sub>3</sub>

## RESULTS AND DISCUSSION

Wet granulation process was used to prepare the Calcium Carbonate and vitamin D<sub>3</sub> tablets by using different types of excipients (table 1). Tablet properties were evaluated by performing various tests. The result of weight variation test was + 0.76% and -1.42%. The weight variation test is alternative to content uniformity test that assure the therapeutic utility [13]. Weight variation test is an also an indicator of variations in the drug content [14]. Standards and specifications have given in Pharmacopoeias that provide permissible limits for weight variation. Result of length, width and thickness was 19.4 mm, 9.2 mm and 5.9 mm respectively whereas the permissible limit according to BP is 19.2 mm – 19.4 mm for length, 9.0 mm – 9.2 mm for width and 5.6-6 mm for thickness. The result of hardness was 10 kg (permissible limit is not less than 4.0 kg) which meet the permissible limit. Friability test indicates the mechanical strength. According to Pharmacopoeia friability for compressed tablet is not more than 1.0%. The result of Calcium and Vitamin D<sub>3</sub> tablet was 0.14%. After physical tests the tablets were subjected to chemical tests. Assay, disintegration and tests were carried out for evaluation of chemical properties. Availability of a drug for dissolution and absorption is determined by evaluation of disintegration [15]. The result showed that tablets took 5 minutes to disintegrate (permissible limit is not more than 15 minutes). Content of Cholecalciferol was determined by HPLC method and the result was 202.4 IU (permissible limit is 180.0 IU -330.0 IU). The Calcium content was assayed by Titrimetric Method and result was 497.07 mg (permissible limit is 450.0 mg -550.0 mg). All results are given in table 2.

### Calculation:

#### Content of elemental Calcium:

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

$$= 15.1 \times 0.986 \times 2.004 \times 1414.4 / 84.9 \text{ mg/tablet}$$

$$= 497.07 \text{ mg/tablet}$$

V= Volume of 0.05M disodium EDTA in ml = 15.1

F = Factor of the titrant = 0.986

W = Average weight of tablet in mg = 1414.4

WT = Weight of sample in mg = 84.9 mg

#### Content of Cholecalciferol :

$$\frac{AT}{AS} \times \frac{WS}{100} \times \frac{2}{50} \times \frac{50}{WT} \times \frac{Ps}{100} \times W \text{ mg/tablet}$$

$$= 28304/28455 \times 99.0/100 \times 2/50 \times 50/1400 \times 100000/100 \times 1414.4 \text{ mg/Tablet}$$

$$= 2.024 \text{ mg/Tablet}$$

$$= 202.4 \text{ IU ( 2 mg = 200 IU)}$$

Where,

AT = Area of sample preparation = 28304

AS = Area of standard preparation = 28455

WT = Weight of sample in mg = 1400

WS = Weight of Cholecalciferol(Vitamin D<sub>3</sub>) standard in mg = 99.0 mg

Ps = Potency of Cholecalciferol(Vitamin D<sub>3</sub>) standard (100000 IU)

W = Average weight of tablet = 1414.4 mg

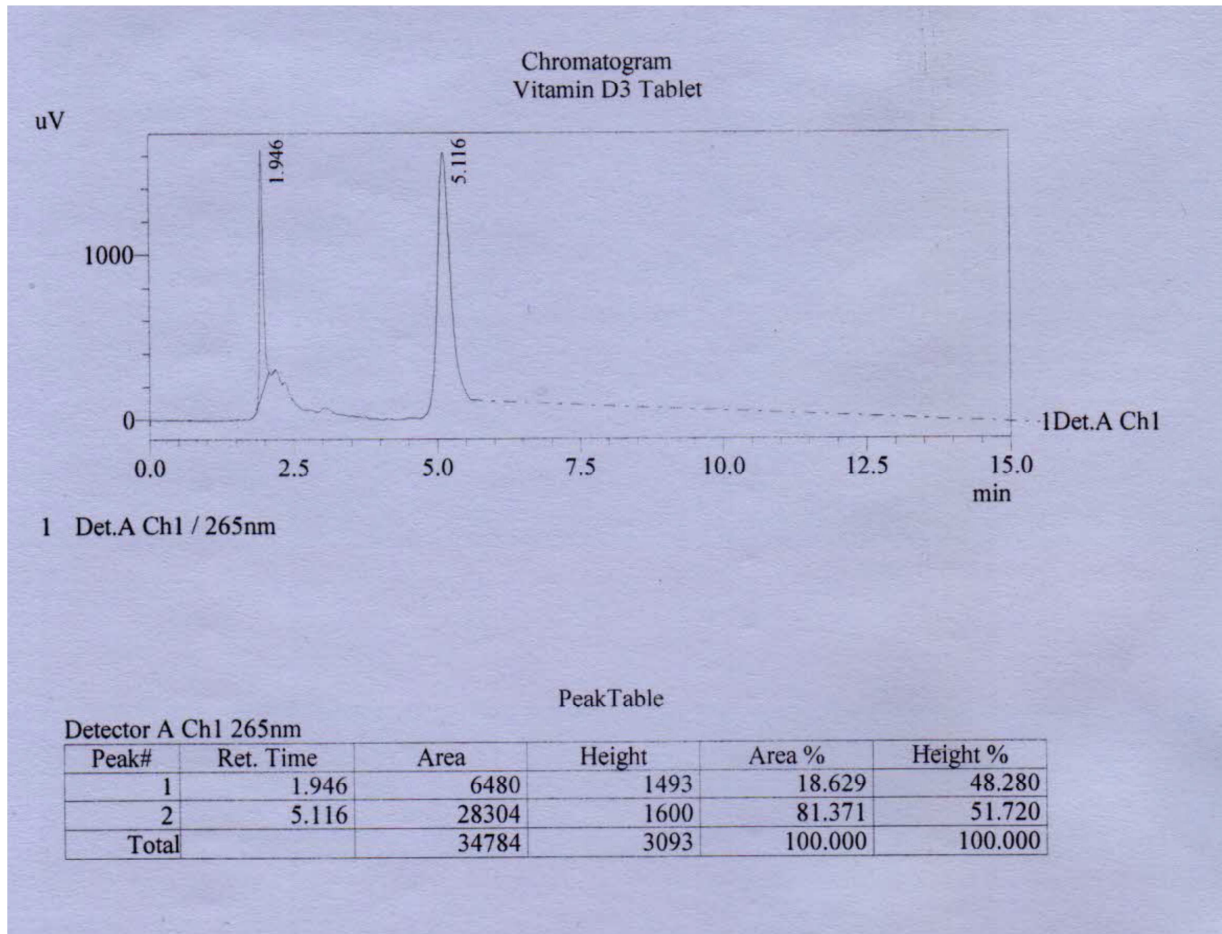


Figure1: Chromatogram of Vitamin D3 tablet(sample)

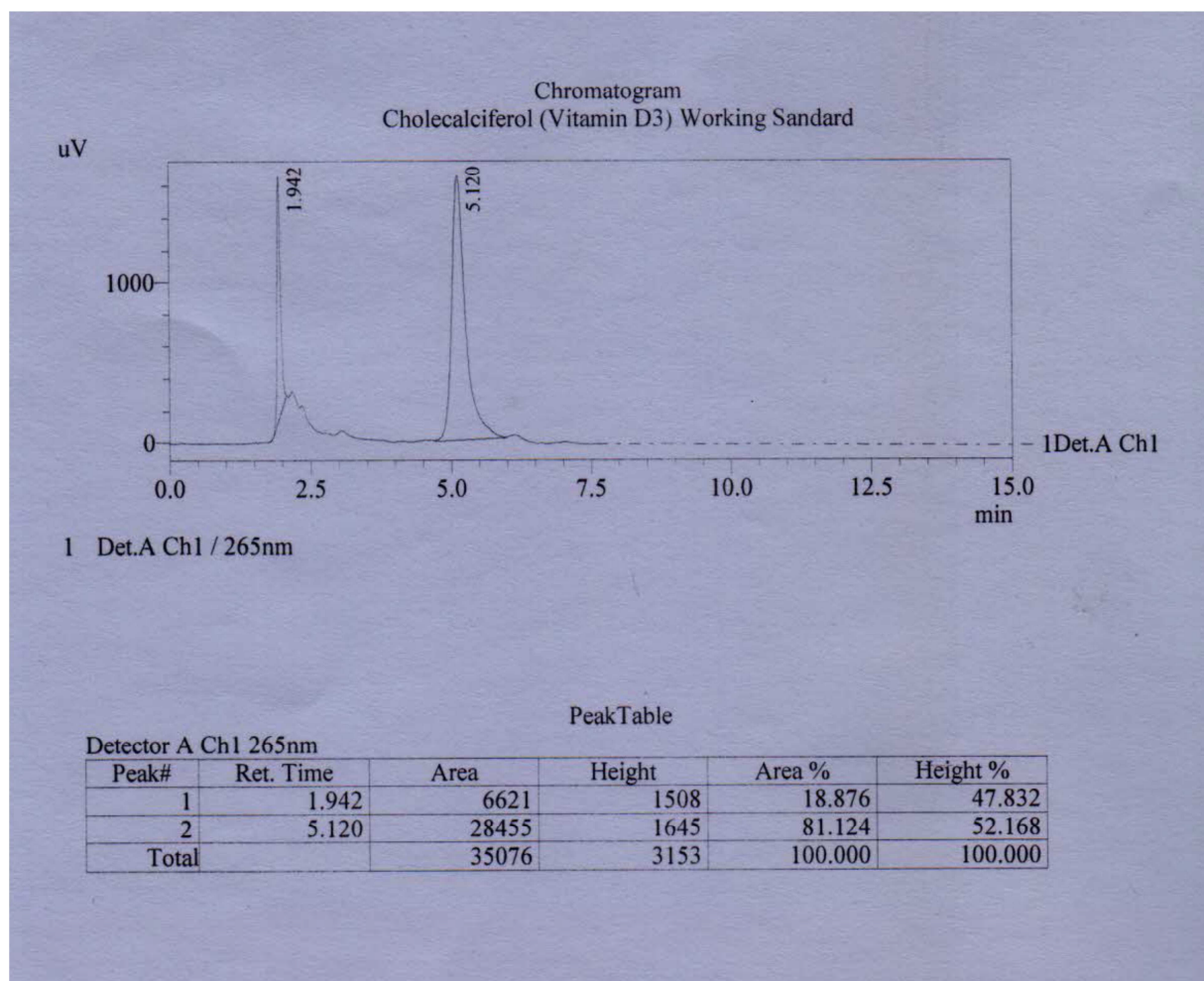


Figure 2: Chromatogram of Vitamin D3 tablet(Standard)

Table 2: Physical and Chemical properties of Calcium and Vitamin D3 tablets			
Sl.No.	Tests	Specifications	Results
1	Average weight /tablet	1388.7 mg to 1445.3 mg	1414.5 mg
2	Weight variation	$\pm 5.0\%$	+ 0.76% and -1.42%
3	Length	19.2 mm – 19.4 mm	19.4 mm
4	Width	9.0 mm – 9.2 mm	9.2 mm
5	Thickness	5.6 mm-6.0 mm	5.9 mm
6	Hardness	Not less than 4.0 kg	10 kg
7	Friability	Not more than 1.0%	0.14%
8	Disintegration time	Not more than 15 minutes	5 min
9	Assay:	450.0 mg -550.0 mg	497.07 mg
	a. Content of elemental Calcium per tablet		
	b. Content of Vitamin D3 per tablet	180.0 IU -330.0 IU	202.4 IU

### CONCLUSION

In the present work, vitamin D3 and calcium tablets were manufactured successfully that fulfills all the pharmacopoeial limits. This type of study not only for this combination but also be done on other drugs. Present data would be used as a reference for future work.

## REFERENCES

- [1] Vieth R, Ladak Y, Walfish PG. *J Clin Endocrinol Metab.* **2003** Jan;88(1):185-91.
- [2] Pérez-López FR. Vitamin D and its implications for musculoskeletal health in women: An update. *Maturitas.* **2007**, Jun 28.
- [3] Lappe J, Travers-Gustafson D, Davies K, Recker R, Heaney R. *American Journal of Clinical Nutrition.* **2007**, June 8;85(6):1586-1591.
- [4] Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. *J Clin Endocrinol Metab.* **2007** May 29.
- [5] Maghbooli Z, Hossein-Nezhad A, Karimi F, Shafaei AR, Larijani B. *Diabetes Metab Res Rev.* **2007** Jul 2.
- [6] Wilkins CH, Sheline YI, Roe CM, Birge SJ, Morris JC. *Am. J Geriatr Psychiatry.* **2006** Dec;14(12):1032-40.
- [7] Pérez-López FR. Vitamin D and its implications for musculoskeletal health in women: An update. *Maturitas.* **2007** Jun 28.
- [8] Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Abtei Pharma Vertriebs GmbH on the scientific substantiation of a health claim related to Calcium plus Vitamin D3 chewing tablets and reduction of the risk of osteoporotic fractures by reducing bone loss. *The EFSA Journal*, **2009**, 1180, 1-13.
- [9] Avenell A, Gillespie WJ, Gillespie LD, O'Connell DL. *The Cochrane Database of Systemic Reviews* 3, **2005**, CD000227.
- [10] Boonen S, Lips P, Bouillon R, Bischoff-Ferrari HA, Vanderschueren D, Haentjens P. *The Journal of Clinical Endocrinology and Metabolism* **2007**,92 (4), , pp. 1415-1423.
- [11] Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P. *The Cochrane Database of Systemic Reviews* 2, **1998**, CD000952
- [12] Tang BMP, Eslick GD, Nowson C, Bensoussan A. *Lancet*, **2007**, 370 (9588), pp. 657-666.
- [13] Katori, N., Aoyagi, N. and Kojima, S. *Chem. Pharm. Bull.* (Tokyo), **2001**, 11: 1412-1419.
- [14] Rawlins, E.A. (ed). *Bentley's Text book of Pharmaceutics*, 8th ed. Bailliere Tindall, London, **1995**, pp.289-290.
- [15] Block, L.H. (2007). *Pharmaceutical Principles and Drug Dosage Forms*. In: Shargel L, Mutnick AH, Souney PF and Swanson LN (eds.) *Comprehensive Pharmacy Review*, 6th ed. Lippincott Williams and Wilkins, New York, **2007**, p.68.