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Nano vitamin D₃ chewable tablet

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ABSTRACT

The present study was conducted to develop Nano Nano Vitamin D₃ chewable tablet. The experiment was designed accordingly ZEON F&D SOP for the Nano Vitamin D₃ chewable tablet. ZLL/F&D/024. Five formulations were carried out for development of Nano Vitamin D₃ to check the overall acceptability. For the development of Nano Vitamin D₃, experimental design with the active ingredient (Nano Vitamin D₃ powder), lubricant, glidant, diluents, and flavour produced different combinations that were studied using pre and post evaluation parameters. The methodology of Nano Vitamin D₃ chewable tablets was carried out by dry mixing method. The chewable tablet was compressed by using tablet compression machine. A Nano Vitamin D₃ chewable tablet was orange granular powder. Nano Vitamin D₃ was the main factor of the chewable tablet, Nano increases the bioavailability of Vitamin D₃ which possess a significant role in a various disease like Osteoporosis, Muscle weakness, Hypertension, Multiple sclerosis, Malabsorption, Rickets, Cancer, Rheumatoid Arthritis(RA), Diabetes, Tuberculosis (TB) etc.

Keywords: Nano, Vitamin D₃, Chewable, Tablet.

1. INTRODUCTION

Administration of drugs through oral route is the most common and the easiest way to administer a drug. But it is a challenge in children who have not yet learned to swallow tablets. Hence it was decided to formulate Nano Vitamin D₃ chewable tablet to improve the compliance in children. Chewable tablets are the tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. Geriatric and pediatric patients and traveling patients who may not have ready access to water are most need of easy swallowing dosage forms like chewable tablets.[1]

1.1 General formulation factors

Various factors involved in the formulation of chewable tablets. The major formulation factors are flow, lubrication, disintegration, organoleptic properties, compressibility, compatibility, and stability, which are common to regular (swallowed) and chewable tablets; however, organoleptic properties of the active drug substances are the primary concern here.[2]

1.2 Vitamin D

Vitamin D is a liposoluble atom and its real capacities are the expansion of intestinal retention of calcium and advancement of typical bone arrangement and mineralization. Vitamin D has two principle substance frames, vitamin D₃ (cholecalciferol) or vitamin D₂ (ergocalciferol). The synthetic structures appear in figure 1.[3]

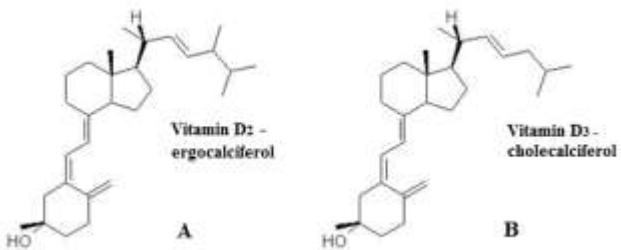


Fig.1. (a)ergocalciferol, (b)colecalciferol[4]

1.2.1 Vitamin D₃

Vitamin D needs to tie to a receptor, known as the vitamin D receptor or VDR, which enables the association with its hereditary impacts, and furthermore have been distinguished in a few tissues and cells. Vitamin D goes in the blood limited to an α -globulin and is available in two fundamental compound structures, specifically ergocholecalciferol or actuated ergosterol or vitamin D₂ and cholecalciferol or enacted 7-dehydrocholesterol or vitamin D₃.[5]

1.2.2 Vitamin D₃ metabolism

Cholecalciferol is inert and must be metabolized in the liver and the kidney through two hydroxylation processes to be converted to its active form. Thus, the first step of this activation, the hepatic 25-hydroxylation, inserts a hydroxyl group in C25 of cholecalciferol, thereby creating 25-hydroxyvitamin D₃ (25-OH-D₃). This step of 25-hydroxylation is mediated by a 25-hydroxylase enzyme (CYP2R1). Later in the kidney, 25-hydroxyvitamin D₃ 1 α -hydroxylase (CYP27B1) enzyme is responsible for the insertion of one more OH group into the C1 of the A ring, converting it into calcitriol. In Figure 2 also, the overall process of vitamin D activation is schematized.[6]

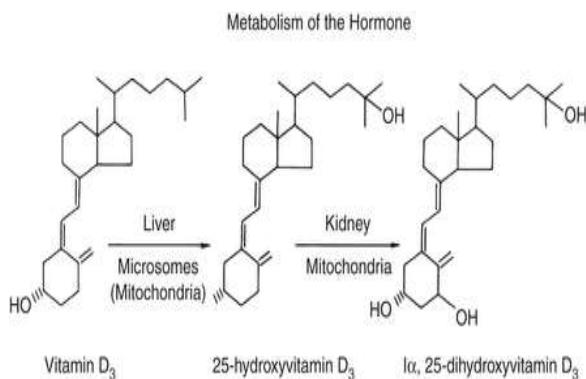


Fig.2. Representation of cholecalciferol three different chemical structures: (a) Calcio, (b) calcidiol, and (c) calcitriol.[7]

1.2.3 Clinical applications of Vitamin D₃

Clinical applications of Vitamin D₃ are-

- Osteoporosis
 - Cancer
 - Multiple sclerosis
 - Autoimmune disease
 - Hypertension
 - Heart disease
 - Diabetes
 - Sun damage
 - Neurological disease

- Psoriasis
- Tuberculosis
- Asthma[8]

1.3 Nanotechnology

The greater surface area of nanoparticles per mass unit, they are expected to be more biologically active than larger sized particles of the same chemical composition. Nanoparticles sized between 1 and 100 nanometres[9] The nano- and micro-encapsulation of vitamin D3 towards a therapeutic used. The micro-encapsulation of cholecalciferol as a drug model or as a nutrient supplementation. Encapsulated cholecalciferol into cellulose acetate microspheres as an anti-oxidizing agent to enhance pancreatic islet cell viability and function and bioavailability.[10]

2. METHODOLOGIES

2.1 Material

Nano Vitamin D₃, Diluent, color, Flavour, Sweetener, Lubricant, and Glidant purchased from by department of Zeon Lifesciences Pvt. Ltd. from different vendors.

2.2 Method

All powder compounds were accurately weighted, passed through a standard sieve(sieve no 20) except glidant and lubrication and which is passed by standard(sieve no 40) and thoroughly blended all powder for 5 min. After being mixed powders were evaluated for bulk density and tapped density, compressibility index, the angle of repose and moisture content. Chewable tablets were prepared by dry granulation method using rotary tablet compression machine(Accura tablet punching machine). Five batches (F1, F2, F3, F4, F5) of orange color tablets with an average mass of 1400 mg were obtained. The completed composition of the tablets of five batches.

2.2.1 Granulation

Granulation is the process in which primary powder particles are made to adhere to form larger, multi-particles entities called granules. Pharmaceutically granules have a size range between 0.2 to 4.0 mm. Granulation is used to improve flow and compressibility of powders and to prevent segregation of the blend components. Granulation is mainly done by using two techniques.

- Dry granulation
- Wet granulation
- Direct Compression

2.3 Formulation Development

The experiment was designed accordingly **ZEON F&D SOP** for the chewable tablet ZLL/F&D/SOP/024. Five trials were performed to optimization for **Nano Vitamin D3 Chewable Tablets**.

Table .1 – List of ingredients used in the formulation of Nano Vitamin D₃ Chewable Tablet

S.N o	Ingredien ts	Formulation				
		(g)	F1	F2	F3	F4
1.	Nano Viatmin D3 (Active Agent)	120.0 0	120.0 0	120.0 0	120.0 0	120.00
2.	Diluent	15	15.10	15.20	15.25	15.30
3.	Colour	0.50	0.50	0.50	0.50	0.50
4.	Flavour	0.90	0.80	0.85	0.90	0.90
5.	Sweetner	0.50	0.60	0.65	0.50	0.50

6.	Lubricant	1.20	1.20	1.00	1.30	1.40
7.	Glidant	1.40	1.40	1.40	1.40	1.40

3. EVALUATION OF CHEWABLE TABLETS

3.1 Pre-compressional studies of the powder blend

In the development of new dosage form, the pre-formulation study is the prior step in the potential drug development. It is the principal investigation in the drug development to obtain information on the known properties of the compound and the proposed development schedule. So, this pre-formulation investigation may merely confirm that there are no significant barriers to compound development. Following pre-compressional parameters were studied like the angle of repose, bulk density, tapped density, compressibility indices etc.

3.1.1 Angle of repose

The angle of repose of the powdered blend was determined by the funnel method. The accurate weight granules were taken in a 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 onto the surface. The diameter of the powder cone was measured using the following equation.

$$\phi = \tan^{-1} (h/r)$$

3.1.2 Bulk density

Both loose bulk density (LBD) and tapped density were determined. A quantity of the powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial volume was absorbed, the cylinder was allowed to fall under its own weight onto a hard surface. From the height of the 2.5 cm. LBD and TBD were calculated using the following formulas.

LBD(Loose Bulk Density) = Mass of powder/volume of the packing.

TBD(Tapped Bulk Density) = Mass of powder / tapped volume of the packing.

3.1.3 Compressibility index

The compressibility of the powdered blend was determined by Carr's compressibility index.

Carr's index (%) = (TBD - LBD) / TBD × 100

3.2 Post-compressional studies of prepared tablets

The tablets were evaluated for various parameters after consideration of pre-formulation to overcome errors during formulation preparation. These are like appearance, thickness, weight variation, hardness, and friability. Physical appearance. The general appearance of the tablet was studied visually in shape, color, texture, and odor.

3.2.1 Weight Variation

Weight variation test is run by weighing 20 tablets individually, calculating the average weight and comparing individual tablet weight to the average. The weight variation test would be a satisfactory method of determining the drug content uniformity of tablets.

3.2.2 Friability

The friability of the tablets was determined using Roche friabilator. This device subjects the tablets to the combined effect of absorption and shocks in a plastic chamber revolving at a height of 6 inches in each revolution. A pre-weighted sample of taste was placed in the friabilator and was subjected to 100 revolutions. Tablets were degusted using a soft muslin cloth and reweighted. The friability (F) is given by the formula.

$$F = (1-w_0/w) \times 100$$

Where w_0 is the weight of the tablets before the test and w is the weight of the tablets after the test.

3.2.3 Hardness

The strength of tablet is expressed as tensile strength (Kg/cm^2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester).

3.2.4 Thickness

The tablet thickness was calculated by Vernier callipers. Tablet was put in between two jaws vertically and measured thickness and 6 tablets were used for this test and expressed in mm.

4. RESULTS AND DISCUSSION

The Chewable Nano Vitamin D₃ tablet was formulated by dry granulation method. This technique was used for a tablet which minimizes processing steps and eliminated wetting and drying process. The physiochemical property shows satisfactory results by a tablet which are within the range of prescribed standards required for investigation of the present study. Tablets were examined on the basis of weight uniformity, friability, hardness, thickness etc.

4.1 Pre- compressions studies of the powder blend

Table.2- The powder blend was evaluated for various parameters and their results

Pre-compression parameter	Formulation code				
	F1	F2	F3	F4	F5
Angle of repose(θ)	24.2	22.3	22.4	23.5	24.2
Bulk density(g/ml)	0.30	0.33	0.31	0.35	0.34
Tapped density(g/ml)	0.40	0.43	0.42	0.44	0.45
Carr's index	25	23.1	26.1	20.4	24.4

4.2 Post-compression studies of tablet

Table.3- Post – compression results of tablet

Post-compression parameter	Formulation code				
	F1	F2	F3	F4	F5
Thickness (mm)	7.36	7.28	7.36	7.34	7.54
Hardness (kg/cm^2)	2.7	2.5	2.6	2.3	2.2
Weight variation(mg)	1263	1273	1384	1398	1403
Friability (%)	0.41	0.36	0.40	0.32	0.31

5. CONCLUSION

From the above study, we conclude that the nano Vitamin D₃ chewable tablets were prepared by dry granulation method and gave the satisfactory and acceptable result. Nano Vitamin D₃ was the main factor of the chewable tablet, nano increase the bioavailability of Vitamin D₃ which posses significant role in a various disease like Osteoporosis, Cancer, Multiple sclerosis, Autoimmune disease, Hypertension, Heart disease, Diabetes, Sun Damage, Neurological disease, Psoriasis, Tuberculosis, Asthma. According to the results obtained from all batches formulation (F5) shows for Carr's index and angle of repose, flowability were better compared with other batches. According to the obtained results and our requirements, batch F5 was our choice for further development of the commercially applicable product.

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