

## Research Article

# Review on Formulation Development and Evaluation of Water Soluble Vitamin D<sub>3</sub> Granules

Dilkhush jain\* Sankar Narayan Bunia, Kirtan Pandya, Suresh jakhar and Abhiney Rana

Shree Balaji College of Pharmacy, Jaipur, Rajasthan, India.

**ABSTRACT**

The aim of this investigation was to develop a water soluble vitamin D<sub>3</sub> granules. Vitamin D, a fat soluble vitamin is practically insoluble in water and used in treatment of rickets and osteoporosis. Solubility is rate limiting step for absorption of vitamin D leading to poor bioavailability. Currently vitamin d is available in form of tablet along with calcium supplements and in sachet as water insoluble granules. It has been recommended to take by dispersing in milk. Since vitamin d is insoluble in water it disperse poorly in milk led to non homogenous delivery until contents were washed with additional amount of water. This may lead to patient non-compliance. Its hydrophobicity further limits its absorption and thus bioavailability. Thus if vitamin D is administered in solubilized form in such a way that resist precipitation post dilution with water may result in its improved bioavailability. Thus objective work presented in this thesis is to prepare water soluble granule of Vitamin D<sub>3</sub>. enhance the solubility of Vitamin D<sub>3</sub> by using different surfactant, co-surfactant and oils .as to increase its which is rate limiting step in absorption of water Insoluble drug and ultimately to increase bioavailability and easy to carry to anywhere through sachet easy to administration by own hand in oral route its simply no time consume and not like painful injection .and its better than other routes and formulation .

**Keywords :** Solubility, Bioavailability, Surfactant, Micro emulsion system.

**INTRODUCTION**

Oral route of administration has received maximum attention with respect to research on physiological and drug constraints as well as design and testing of products. This is because there is more flexibility in dosage form design for the route than for other routes. The need for delivering drugs to patients effectively and with fewer side effects is main aim of development of new drug delivery systems. So keeping the aim of ndds in mind a novel approach is developing vitamin D<sub>3</sub> water soluble granules. Vitamins are essential organic nutrients required in very small amounts for normal metabolism, growth and physical well-being. Most vitamins are not made in the body, or only in insufficient amounts, and are mainly obtained through food. When their intake is inadequate, vitamin deficiency disorders are the consequence. Vitamin D is a steroid vitamin, a group of fat-soluble prohormones, which encourages the absorption and metabolism of calcium and phosphorous. People who are exposed to normal quantities of sunlight do not need vitamin D supplements because sunlight promotes sufficient vitamin D synthesis in the skin. The cholecalciferol is the other name of the vitamin D<sub>3</sub>. Vitamin D<sub>3</sub> is made in the skin when 7-dehydrocholesterol reacts with

ultraviolet light at 270-300 nm wavelengths - peak vitamin D<sub>3</sub> production occurs between 295-297 nm. Cholecalciferol is a vitamin D<sub>3</sub>. Vitamin D is important for the absorption of calcium from the stomach and for the functioning of calcium in the body. Cholecalciferol is used to treat or prevent many conditions caused by a lack of vitamin D, especially conditions of the skin or bones. Vitamin D for humans is obtained from sun exposure, food and supplements. It is biologically inert and has to undergo two hydroxylation reactions to become active in the body.

**Experimental Work**

Drug : Vitamin D<sub>3</sub> (Cholecalciferol)  
Surfactant : Cremophore Rh40, Tween80  
Antioxidant: Citric Acid Monohydrate IP  
Diluents: Lactose DCL21, Mannitol  
Binder: PVPK-30, Starch  
Flavour And Sweetner: Aspartame, Neotem, Pineapple flav.  
Water soluble vitamin D<sub>3</sub> granules were prepared by wet granulation technique.

**Dispensing**

The required quantity of Vitamin D<sub>3</sub>, Cremophore RH40, Citric acid, propylene glycol, Iso propyl alcohol, PVPK-30, Lactose

DCL21 ,Aspartame , Pineapple flavour were weighed accurately.

### Sifting

The Vitamin D3 was passed through 40# sieve, Lactose DCL21 were passed through 40# sieve.

### Granulation

For wet granulation, the binder solution was prepared by dissolving PVP-K-30 in IPA and stirred it until it completely dissolved. Granulation was done in Rapid Mixer Granulator (RMG). Parameters of Rapid Mixer Granulator for wet granulation are shown in Table 7.1.

**Table 1: Parameters of Rapid Mixer Granulator for wet granulation**

Process	Time (min)	Speed of Impeller	Speed of Chopper
Dry mixing	10	75 rpm	Off
Binder addition	2	150 rpm	Off
Kneading	1	150 rpm	1500 rpm

Unload the material into in process container .pass the wet mass through oscillating granulator fitted with #16 screen and collect the granules in plastic tub.

### Drying

- Keep the wet granules spread in thin layer in trays aside for 30 min.
- Transfer the wet granules to the tray grayer and dry at a ambient temp. for 4 hours .
- Set the tray dryer temp. at 40c for and dry the granules at 40c for 24 hours. And check the moisture content. it should be between 3.0-5.0% w/w by loss on drying method using halogen moisture balance at 105c. if it is more

dry further until the moisture content is 3.0 to 5.0%w/w .

- Check moisture content of the granules by loss on drying method using halogen moisture balance.
- Limit – 3.0 -5.0 %w/w by loss on drying using halogen moisture balance at 105c .

### Dry Screening

- Pass the granules through sifter using # 12 sieve.
- Tap the above granules from #20 s.s sieve and collect the oversize granules in tight , light resistant container lined with sachet and label the container.

### Evaluation Parameters for vitamin D3 granules

#### 1) Flow of Vitamin D3 granules

#### Bulk Density (BD)

$$\text{Bulk density} = \text{Weight of powder} / \text{Bulk volume} \dots\dots\dots (1)$$

#### Tapped Density (TD)

$$\text{Tapped Density} = \text{Weight of powder} / \text{Tapped volume} \dots\dots\dots (2)$$

#### Carr's index & Hausner's ratio

$$\text{Carr's Index (\%)} = [(TD-BD) \times 100] / TD \dots\dots\dots (3)$$

$$\text{Hausner's Ratio} = TD / BD \dots\dots\dots (4)$$

#### Angle of Repose

$$\tan \alpha = h/r \dots\dots\dots (5)$$

Where, h = Height of heap in cm  
r = Radius of heap in cm

**2) Particle size analysis**

Particle size of the optimized formulation is checked at different time interval with respect to different environmental conditions by using Malvern zeta sizer instrument.

(containing 10 mg of Vitamin D3) was diluted with 10 ml of methanol. Then further diluted with ethanol and content was analyzed spectrophotometrically using UV/Visible spectrophotometer (Shimadzu 1700) at 265 nm against the corresponding blank.

**3) Stability studies**

The I.C.H. guidelines give the following definition for accelerated stability tests.

$$\text{Drug content (\%)} = \frac{\text{Actual amount of drug}}{\text{Theoretical amount of drug}} \times 100$$

**4) Determination of Drug Content**

60 g of the developed water soluble vitamin d3 granules formulation

**RESULTS AND DISCUSSION****1) Flow of Vitamin D3 granules****Table 2: Flow parameters (Granules evaluation)**

Bulk Density(gm/cm <sup>3</sup> )	Tapped Density (gm/cm <sup>3</sup> )	Angle of Repose	Carr's Index	Hausner's Ratio
0.431	0.538	29.16	20	1.250

**2) particle size analysis****Table 3: Particle size of Formulation at different time interval at different temperature condition**

Formulation	Time	2-8°C (d.nm)	40°C/75RH (d.nm)	25°C/60RH (d.nm)	R.T. (d.nm)
F5	0(initial)	265.7	242.6	235.3	255.2
	1 month	272.2	242.8	237.3	260.3

**3) Drug content of Formulation at different time interval at different temperature condition in table 4**

Formulation	Time	Result
F5	0(initial)	105.7%
	1 month	101.1%

Drug content of the optimized SEDDS formulation batch (N/FD/024/19) was found to be 101.1 %.

**4) Optimization of composition of Vitamin D3 granules**

Formulation code	Optimization by physical parameter		
	Water solubility	Test	Flow of granules
F1	Turbid	Good	Poor
F2	Clear	Bitter	Good
F3	Turbid	Bitter	Good
F4	Turbid	Bitter	Good
F5	Clear	Good	Good

Above table F5 is the better composition than other composition, because F5 shows better solubility in water and give pleasant taste with pineapple flavour, no bitterness was observed and an appropriate flow of granules for better absorption and for better patient compliance. F5 composition was selected for best formulation of water soluble vitamin D3 granules

**5) STABILITY STUDY****Physical observation****Table 5: Physical observation of optimized formulation**

Formulation	Withdrawal Time	2-8°C	40°C/75RH	25°C/60RH	R.T.
F5	0(initial)	√	√	√	√
	15 day	√	√	√	√
	1 month	√	√	√	√

√ - Stable, X – unstable

**CONCLUSION**

The water soluble Vitamin D3 granules were prepared with immediate release require for onset of action. Preformulation study was carried out in drug solubility, micromeritic property and drug-excipients compatibility study. Drug-excipients compatibility study was shown that there was no interaction between drug and excipients. The Surfactant selected for solubility in water. The citric acid and propylene glycol are selected for as a anti-oxidant or as a solvent. We mainly performed for optimization of surfactant concentration and the ratio of surfactant with drug in formulation. Stability study of granules with sachet packaging was shown that there was no major effect of temperature and relative humidity on assay .So, Water soluble vitamin D3 granules is stable formulation. Above table F5 is the better composition or formulation than other composition. because F5 have the better solubility in water and better give test with pineapple flavour, no bitterness was came .and also have nice flow of granules for better absorption and for better patients compliance . so we select the F5 composition for best formulation of water soluble vitamin D3 granules . in other formulation and composition with combination of other different-2 oils, surfactant and co surfactant having bitterness was came and water solubility is not properly came so F5 give best composition for water soluble vitamin D3 granules .

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