D-Cure®

25,000 IU Oral Solution
Equivalent to 0.625 mg of Cholecalciferol

67.4% of Malaysian Healthy Adults are Vitamin D Deficient[2]
Prevalence is higher in FEMALES[2]

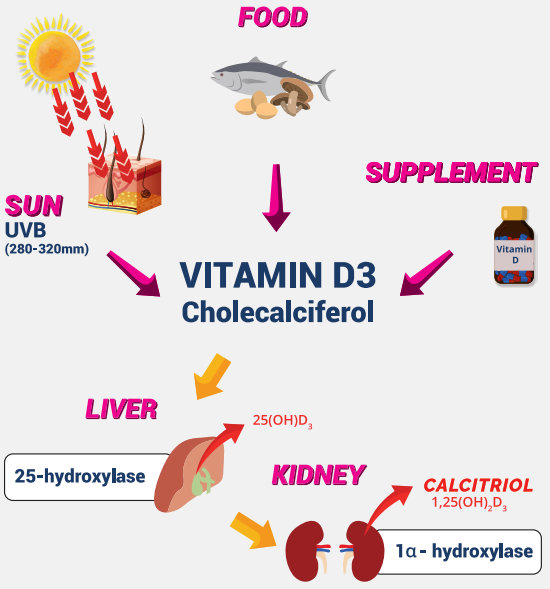
VITAMIN D DEFICIENCY?

Risk Factors:

- Inadequate Exposure to Sunlight
- SPF30 Reduces Vitamin D Production by 99%
- Age Above 65 Years Old
- Obese BMI >30 kg/m²
- Darker Skin Tone

MALAYSIA'S 1ST
ORAL HIGH DOSE VITAMIN D3

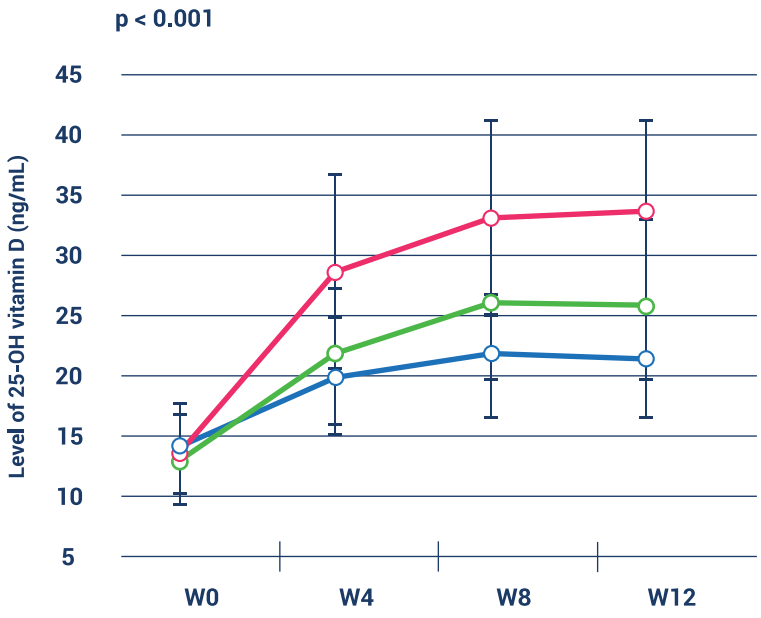
Biotransformation of Vitamin D



Forms of Vitamin D: Cholecalciferol *vs.* Alfacalcidol *vs.* Calcitriol

	Cholecalciferol	Alfacalcidol (1α-hydroxycholecalciferol)	Calcitriol (1α,25-dihydroxycholecalciferol)
Types [3,4]	Inactive Vitamin D	Analogue of Vitamin D	Active Vitamin D
Recommendations [5]	Patients without renal insufficiency	Only in patients with renal insufficiency	
Activation [3,4]	Requires activation by both liver and kidneys	Requires activation (25-hydroxylation) by liver	Active form; Does not require activation by liver nor kidney
Half-Life [3,4]	About 14 – 21 days	About 3 hours	About 4 – 6 hours
Risk of Toxicity [4,6]	Negligible	Common	Significant
Adverse Effects [4,6]	Rare	Hypercalcemia, hyperphosphatemia, hypercalciuria, renal calculi	
Routine Laboratory Monitoring	Not required	Serum Ca/PO_4 Urinary Ca excretion	

98% of Vitamin D Deficient Patients Achieved Serum 25(OH)D_3 level >20 ng/mL as early as week 8 with D-Cure® [7]



Group 3 (n = 50)
Loading dose: 200,000IU at week 0; Followed with: 100,000IU at week 4 and week 8. Total: 400,000IU.

Group 2 (n = 50)
Loading dose: 100,000IU at week 0; Followed with: 50,000IU at week 4 and week 8. Total: 200,000IU.

Group 1 (n = 50)
Loading dose: 50,000IU at week 0; Followed with: 25,000IU at week 4 and week 8. Total: 100,000IU.

Graph 1: Evolution of 25(OH)D Serum Concentrations over Time in a Randomized, Double-blind, Parallel Study.

- Significant increase in 25(OH)D serum concentration was observed between groups after a 12-week treatment period with a mean change from a baseline of 7.72 ± 5.08, 13.3 ± 5.88 and 20.12 ± 7.79 ng/mL for Group 1, Group 2, and Group 3 respectively.
- Greater change in 25(OH)D levels with higher doses of D-Cure®.
- D-Cure® was demonstrated to be safe as no variation in calcium levels and no clinically relevant adverse events were observed between groups after 3 months of treatment.

High dose Vitamin D treatment is PROVEN SAFE

Loading dose of 25,000 IU every week for 8 weeks (total dose of 200,000IU)[8]

	25(OH)D (ng/mL)	Creatinine (µmol/L)	Total calcium (mmol/L)	Phosphate (mmol/L)	Albumin (g/L)	PTH (pmol/L)
Before	8.28 ± 3.36	69.7 ± 19.2	2.32 ± 0.09	1.00 ± 0.18	39.0 ± 3.0	5.5 ± 5.3
After	35.88 ± 10.76*	72.4 ± 24.0	2.34 ± 0.10	0.97 ± 0.17	39.4 ± 2.9	4.0 ± 2.8**

*Note: n=110, *P<0.0001 ; **P<0.01.*

Table 1: Comparison of laboratory values at baseline and 10 days after final dose of cholecalciferol.

"In this study, no toxic effects were observed, hypercalcemia did not develop, Vitamin D levels were below the danger range, and complete suppression of PTH levels was not observed."[8]

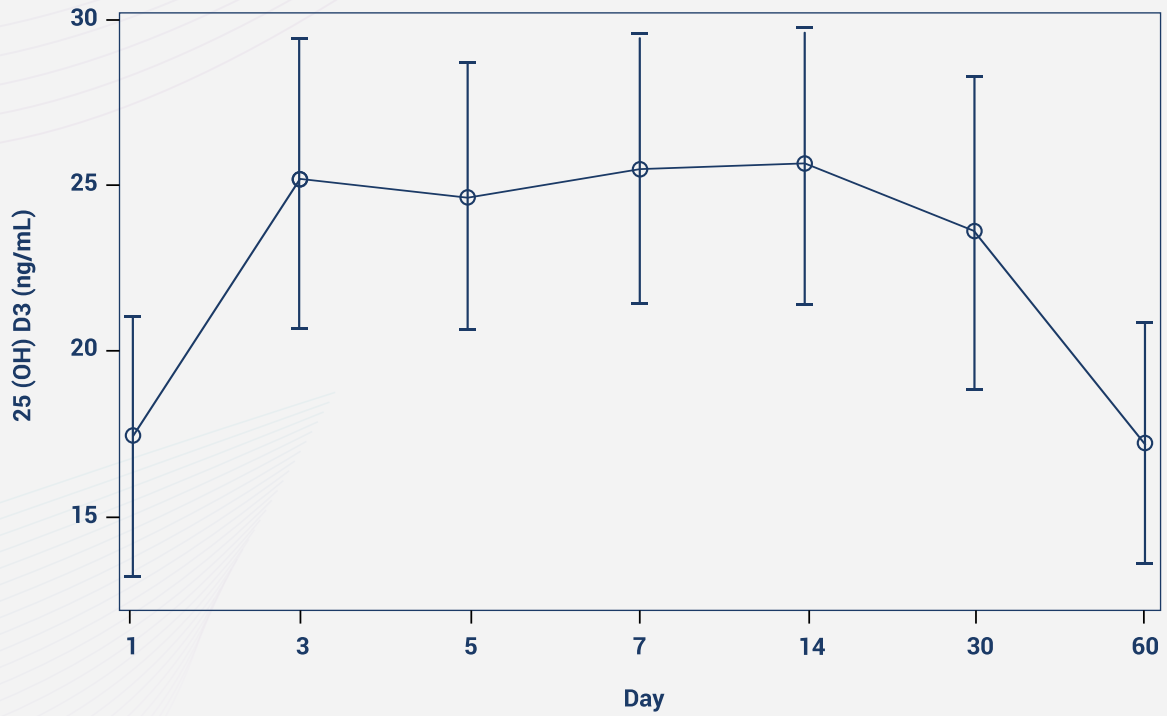
Does High Dosage of Vitamin D Causes Toxicity?

Vitamin D Toxicity only occurs when

- **>150 ng/mL serum level of 25-hydroxyvitamin D**
- **Doses ≥ 50 000 IU/day for several weeks or months**

Multiple studies on D-Cure® have observed highest value of serum level of 25(OH)D_3 achieved ranges from **35 ng/mL - 68 ng/mL,** which is **far from the concentration that might results in toxicity.**[7,9,10]

Level of 25(OH)D Rapidly Increased by Day 3 & Sustained over 30 Days with Single Administration of D-Cure® 50,000IU[11]



Graph 2: Evaluation of serum 25(OH)D concentrations following a single dose of D-Cure® 50,000IU.

Serum concentration of 25(OH)D rapidly increased after three days (25.1 ± 4.3 ng/mL), reached a plateau from day 3 to day 14 (25.6 ± 4.3 ng/mL) and decreased until day 60.

D-Cure® is the Preferred Choice in Management of Vitamin D Deficiency

- **1st oral high dose Vitamin D3 in Malaysia**
- **Clinically effective to increase 25(OH)D level from deficiency to sufficiency in 3 months period[8]**
- **Safe and well-tolerated**
- **Reduces burden of daily dosing**
- **Better patients' compliance with monthly dosage**
- **Easy and safe to use**
- **Integrity**
  (plastic twist ampoules are incomparably more resistant)

Brief Prescribing Information

D-Cure 25,000 IU oral solution

Composition: 1 ml solution (1 single-dose oral solution) contains 0.625 mg cholecalciferol, equivalent to 25,000 IU vitamin D. **Pharmaceutical Form:** Oral solution. Clear, slightly yellow, oily liquid with an orange odour. **Therapeutic indications:** Prevention and treatment of vitamin D deficiency. As an adjunct to specific therapy for Osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. **Posology and Method of Administration: Paediatrics:** Prevention of deficiency 0-1 years 25000 IU (1 single-dose oral solution) every 8 weeks. Prevention of deficiency 1-18 years 25000 IU (1 single-dose oral solution) every 6 weeks. Treatment of deficiency 0-18 years 25000 IU (1 single-dose oral solution) once every 2 weeks for 6 weeks (followed by maintenance therapy of 400-1000 IU/day). **Adults:** Prevention of vitamin D deficiency 25000 IU/month (1 single-dose oral solution). Treatment of vitamin D deficiency (<25 ng/ml) 50000 IU/week (2 single-dose oral solution) for 6-8 weeks, followed by maintenance therapy (1400-2000 IU/day may be required; follow-up 25(OH)D measurements should be made approximately 3 to 4 months after initiating maintenance therapy to confirm that the target level has been achieved). As an adjunct to specific therapy for osteoporosis: 25000 IU/month (1 single-dose oral solution). **Contraindications:** Hypersensitivity to the active substance(s) or to any of the excipients, hypercalcaemia and/or hypercalciuria, nephrolithiasis and/or nephrocalcinosis, serious renal impairment, hypervitaminosis D, pseudohypoparathyroidism. **Special Warnings and Precautions:** Patients with impairment of renal function where effect on calcium and phosphate levels should be monitored. Risk of soft tissue calcification should be taken into account; caution in patients receiving treatment for cardiovascular disease; caution in patients with sarcoidosis, due to a possible increase in the metabolism of vitamin D in its active form. Serum and urinary calcium levels should be monitored. Oral administration of high-dose vitamin D (500,000 IU by single annual bolus) was reported to result in an increased risk of fractures in elderly subjects, with the greatest increase occurring during the first 3 months after dosing. **Undesirable effects:** Hypercalcaemia and hypercalciuria (uncommon); pruritus, rash, and urticaria (rare). **Shelf life:** 18 months. **Special precautions for storage:** Do not store above 30°C. Store in the original package, in order to protect from light.

For full prescribing information, kindly refer to the package insert.

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