REVIEW ARTICLE

# Effect of Oral Vitamin D3 Supplements on Lipid Profile and Oxidative Stress in Adult Albino Female Rats

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***Received: 17th Oct, 19; Revised: 25th Nov, 19, Accepted: 15th Dec, 19; Available Online: 25th Dec, 2019***

## ABSTRACT

The present study was designed to show the effect of Vitamin D3 on lipid profile and oxidative stress. The present study used 30 adult albino female rats that distributed to following groups (each group consist 6 rats); control group received ad libidium, second group administrated Vitamin D3 (orally, 8.9µg/kg) for eight weeks, third group administrated Vitamin D3 (orally, 17.8µg/kg) for eight weeks, fourth group (pregnant rats) administrated Vitamin D3 (orally, 8.9µg/k) for eight weeks, fifth group (pregnant rats) administrated Vitamin D3 (orally, 17.8µg/kg) for eight weeks, and then killed. The results showed high significant increased ($P < 0.05$) in levels of lipid profile (total cholesterol, total glyceride, high density lipid (HDL), low density lipid (LDL) very low density lipid (VLDL)), especially in pregnant female rats (third and fifth groups) compared with control group. On the other hand, the results showed significant changes ($P < 0.05$) in levels of malondialdehyde (MDA), Superoxide dismutase (SOD) and catalase especially in pregnant female rats (third and fifth groups) compared with control group. It was concluded that the prolong using and overdose of Vitamin D3 lead to elevated the lipid profile and oxidative stress in rats especially in pregnant female rats.

**Keywords:** Lipid profile, Oxidative stress, Vitamin D3.

International Journal of Drug Delivery Technology (2019); DOI: 10.25258/ijddt.9.4.29

**How to cite this article:** Abdulla, K.N., Ahmed, M.S. and Mohammed, S.R. (2019). Effect of Oral Vitamin D3 Supplements On Lipid Profile and Oxidative Stress In Adult Albino Female Rats. International Journal of Drug Delivery Technology, 9(4): 686-688.

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Vitamin D is critical for bone and mineral metabolism and is effective in the prevention and treatment of rickets and osteomalacia.[1-5] Vitamin D is available in two forms: Vitamin D3 (cholecalciferol) and Vitamin D2 (ergocalciferol). Vitamin D3 is a naturally occurring form and produced in skin cells from 7-dehydrocholesterol underneath the UV light, and Vitamin D2 is produced from the natural sterol, i.e., ergosterol.[6-7] There are numerous sources available for Vitamin D, such as direct sunlight, diet sources (animal and natural sources), and Vitamin D supplements available in the market.[8-9] The active form of vitamin D (1,25(OH)2D3, calcitriol) regulates calcium–phosphate homeostasis through the interaction with vitamin D receptor (VDR). It also has a huge impact on the proper functioning of musculoskeletal, immune, nervous, and cardiovascular systems.[10-12] An increased intake of vitamin D supplements by the general population and a growing number of prescriptions of therapeutic doses (including very high doses) without medical monitoring might result in a greater risk of exogenous hypervitaminosis D, with symptoms of hypercalcemia also known as vitamin D toxicity (VDT).[13-14] So, the aim of this study to demonstrate the toxicity effects of vitamin D.

## MATERIALS & METHODS

### Animal model

Thirty adult female rats (Rattuss norwegicus), (wt: 240-280 with age: 4-6 Mon) obtained from Veterinary college/Baghdad, and kept on a standard pellet diet and water for two weeks before the experiment.

### Experimental design

30 adult female rats were used and distributed in five groups (six rats in each group) as following and administrated orally:

- The control group received normal saline and normal diet for seven days.
- Second group administrated vitamin D3 (orally, 8.9µg/kg) for 8 weeks and then killed.
- Third group administrated vitamin D3 (orally, 17.8µg/kg) for eight weeks, and then killed.
- Fourth group (pregnant rats) administrated vitamin D3 (orally, 8.9µg/kg) for eight weeks and then killed.

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**Table 1:** Levels of lipid profile in all groups

| *Parameters Groups* | *S.Cholesterol mmol/L* | *S. Triglyceride mmol/L* | *HLDL mmol/L* | *LDL mmol/L* | *VLDL mmol/L* |
|---|---|---|---|---|---|
| Control group | 2.15 ± 0.34 b | 1.29 ± 0.27 b | 1.07 ± 0.23 b | 0.82 ± 0.50 a | 0.26 ± 0.05 b |
| Second group | 2.94 ± 0.50 a | 2.34 ± 0.58 a | 1.24 ± 0.24 b | 1.24 ± 0.61 a | 0.47±0.12 a |
| Third group | 3.49 ± 0.33 a | 2.34 ± 0.43 a | 1.47 ± 0.21 a | 1.54 ± 0.31 b | 0.47± 0.09 a |
| Fourth group | 3.01 ± 0.78 a | 1.89 ± 0.07 a | 2.06 ± 0.12 a | 0.78 ± 0.44 b | 0.38 ±0.01 a |
| Fifth group | 3.12 ± 0.71 a | 2.04 ± 0.23 a | 2.03 ± 0.33 a | 0.89 ± 0.7 b | 0.40 ±0.05 a |

**Table 2:** levels of MDA, SOD, and catalase in all groups

| *Parameters Groups* | *Malondialdehyde µmol/L* | *SOD mmol/l* | *S. catalase U/L* |
|---|---|---|---|
| Control group | 1.79 ± 0.39 b | 147.40 ± 7.3 a | 126.60 ± 13.28 b |
| Second group | 2.50 ± 0.46 a | 148.60 ± 7.80 a | 159.60 ± 11.15 a |
| Third group | 2.64 ± 0.56 a | 150.40 ± 5.44 a | 164.20 ± 11.5 a |
| Fourth group | 2.20 ± 0.38 b | 188.6 ± 9.91 b | 164.20 ± 10.99 a |
| Fifth group | 2.46 ± 0.58 b | 190.2 ± 11.63 b | 168.80 ± 19.78 a |

- Fifth group (pregnant rats) administrated vitamin D3 (orally, 17.8µg/kg) for eight weeks and then killed.

**Prepare of blood solution.**

A 5 mL of blood collected by cardiac puncture under anesthesia and put in test tubes. I was then using centrifugation 5000 cycle/min for 15 min. Sera were taken and stored by deep freezing to estimate the biochemical measurement.

## MEASUREMENTS

### Lipid profile

Total cholesterol and triglyceride were measured by technique according to the instructions of the manufacturer company kit (Randox).[15]

### Oxidative Stress and Antioxidant Parameters

MDA (malonedialdehyied) was measured based on the colorimetric reaction with thiobarbituric acid (TBA) using spectrophotometer.[16] SOD and Catalase was measured by using the procedure of Biovision-USA kits**.**

### Statistical analysis

Data of the study were analyzed by using a statistical program known as Minitab. Data means were compared using Duncan's Multiple Range test. Probability levels of more than 0.05 were regarded as statistically non-significant, whereas values less than 0.05 were considered as significant.[17]

## RESULTS

### Lipid profile

Lipid profile (TC, TG, HDL, LDL, and VLDL) in second and fourth groups show significant changes ($p < 0.05$) compared with the control group while lipid profile in third and fifth groups (pregnant rats) show high significant changes ($p < 0.05$) compared with control group as shown in Table 1.

### Oxidative stress and antioxidants

MDA, SOD, and catalase in second and fourth groups show significant increase ($p < 0.05$) compared with the control group. Also, MDA, SOD, and catalase in third and fifth groups (pregnant rats) show significant changes ($p < 0.05$) compared with the control group, as shown in Table 2.

## DISCUSSION

The results of the present study show significant changes in lipid profiles and oxidative stress. Vitamin D toxicity is usually caused by mega doses of vitamin D supplements — not by diet or sun exposure. That's because our body regulates the amount of vitamin D produced by sun exposure, and even fortified foods don't contain large amounts of vitamin D.[18] In many studies show the overuse of vitamin lead to different changes in liver enzymes (AST, ALT, ALP, and total bilirubin) and liver tissues include: degenerative changes, fibrosis and cirrhosis,[19-21] that may explain the overuse effect of vitamin D on lipid profile in this study. About oxidative stress in this study. The present results show significant changes between groups that administrated with magnesium and control group. Many studies show opposite results compare with results of the present study. Where, vitamin D induces the expression of several molecules involved in the antioxidant defense system, including GSH, GSH peroxidase, and SOD and suppresses the expression of NADPH oxidase.[22-23] The reduction in antioxidant enzymes may be due to the high dose of vitamin D in the current study because the high dose is considered to have a toxic effect on the body's cells.

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