# Effect of Induced Vitamin D Deficiency on The Pancreas of Albino Rats

Thesis

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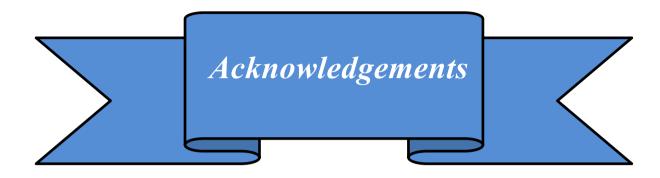
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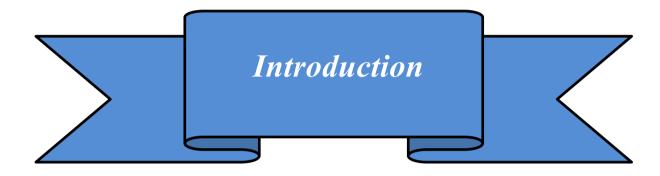
Abbreviations	Full names
1,25(OH)2D	1,25 dihydroxyvitamin D
24,25(OH)2D	24,25 dihydroxyvitamin D
25(OH)D	25-hydroxyvitamin D
AIN	American Institute of Nutrition
ANOVA	Analysis of variance
Са	Calcium ion
DBP	D binding protein
ER	Endoplasmic Reticulum
Fig	Figure
H&E	Haematoxylin and Eosin
HbA1c	Glycated hemoglobin
IU	International unit
P value	Probability value
PP	Pancreatic polypeptide
SS	Somatostatin
T1DM	Type 1 Diabetes Mellitus
T2DM	Type2 Diabetes Mellitus
TPV	Total pancreatic volume
UV	Ultraviolet
UV-B	Ultraviolet medium wave length
VDR	Vitamin D receptor

#### Abstract:

Vitamin D is now considered one of the most important rich fields for research work because of its major role in many aspects of health. Previously it was believed that vit.D concerned only with the homeostasis of Ca but now it is proved to have a crucial role in endocrine and immune system modulation. There are two types of the vitamin, vit.D3 (cholecalciferol) formed mainly in the skin and vit.D2 (ergocalciferol) of diet sources. Both are inactive and need activation in two steps firstly in the liver and then in the kidney. Vitamin D exerts its action via nuclear receptors (VDR) that are present in many tissuses including the pancreatic β cells. The deficiency state of the vitamin is considered to be established when the level of 25(OH) Vit. D reach <20 ng/ml.It is belived that vit.D contributes in the pathogenesis of both types of Diabetes mellitus (DM). It is not only important for insulin secretion but also improve the insulin sensitivity of the target cells. So the aim of the present study was to detect the effect of induced vitamin D deficiency on the blood glucose level and the structure of the pancreas. A total of thirty male Sprague-Dawley albino rats were divided into two groups. *Group I*, consisted of 12 rats as the control group and *Group II*, consisted of 18 rats were further subdivided into group IIa of 9 rats subjected to vit.D deficiency diet for one month and group IIb of 9 rats subjected to vit.D deficiency diet for two months.Light microscopic examination of sections of pancreas stained with H&E, Masson's trichrome and Toluidine blue stains revealed changes in the structure of the islets of Langerhans. These changes were more marked in the rats subjected to the deficient diet for two months than in rats fed the deficient diet for only one month. There were apparent reduction in the number, size and a highly significant reduction in the mean of area fraction % of islets of Langerhans in the two month vit.D deficiency group. Some nuclei showed pyknotic features. Statistical analysis of the blood glucose levels showed non-significant increase in rats subjected to the deficient diet for one month compared with those of the control group, while blood glucose levels showed significant increase in rats subjected to vit.D deficient diet for two months.In conclusion, the present study demonstrated that vit.D deficiency for more than one month can affect the pancreas and produce elevation in the blood glucose level.

## Keywords:

Vitamin D ,, Pancreas ,, Diabetes Mellitus



The variety of health benefits arising from sufficient vitamin D level have generated a strong level of interest in the actions of this vitamin which is a member of the nuclear steroid hormone family and obviously increased the number of requests to laboratories to measure vitamin D level (*Anderson et al.*, 2012).

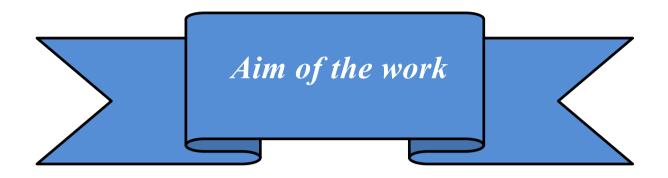
Many Studies have shown that vitamin D can modify both the endocrine and immune system. Furthermore, it plays a critical role in regulating some of the cellular processes like cell proliferation, differentiation, and apoptosis in an autocrine and\or paracrine manner; therefore, it is expected that the vitamin D system is deregulated in some types of cancer (*Hummel et al.*, 2014).

Moreover, the finding that the vitamin D hormone regulates a huge number of genes and their related biological processes improves the awareness into the vital role of vitamin D and sun exposure for human health. Vitamin D has long been known as the sunshine vitamin (*Harinarayan*, 2014). Accumulating epidemiological records linked a low vitamin D nutritional level to highly prevalent diseases such as chronic infections, autoimmune diseases, and cancers (*Janssens*, 2009).

Insufficient vitamin D level has been involved in increasing the risk of many diseases like osteoporosis, cardiovascular disease, diabetes, cancer, and autoimmune diseases such as multiple sclerosis (*Berger et al.*, 2011). Recently, evidence increased on the non-classical role of vitamin D in many autoimmune diseases like rheumatoid arthritis, multiple sclerosis, psoriasis, and also type I diabetes (*Chakhtoura and Azar*, 2013).

Vitamin D receptors present in pancreatic β cells, and vitamin D may increase insulin secretion from them and also improve insulin sensitivity of the target cells (*Thacher and Clarke, 2011*). There is increasing data that suggests that altered vitamin D level and calcium may have an important role in the development of type II diabetes. This obvious role of vitamin D has been suggested on the basis of studies used animals which showed that low vitamin D level was associated with glucose intolerance or diabetes mellitus (*Mitri et al., 2011*).

Today, vitamin D deficiency is considered to be a worldwide health problem. One billion individuals is suggested to have vitamin D deficiency [25(OH) Vitamin D <20 ng/ ml] (*Harinarayan*, 2014). So the aim of the present study became to study the effect of induced vitamin D deficiency on the blood glucose level and the structure of the pancreas.

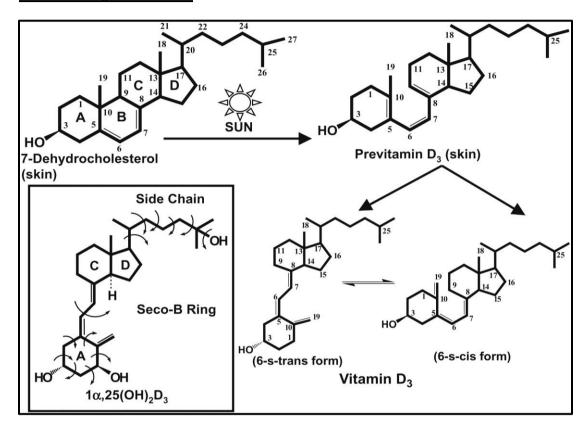


The aim of the work is to investigate the effect of vit.D deficiency on blood glucose level and structure of the pancreas of the albino rat.



## Vitamin D:

### Structure of vitamin D:



**Diagram I:** Diagram showing the molecular structure of vitamin D (*Norman*, 2008).

Vitamin D is classified as a secosteroid as the molecular construction of vitamin D is closely related to that of steroid hormones (e.g. estradiol, cortisol, and aldosterone) in that they have the same root ring structure (Diagram I). Vitamin D2

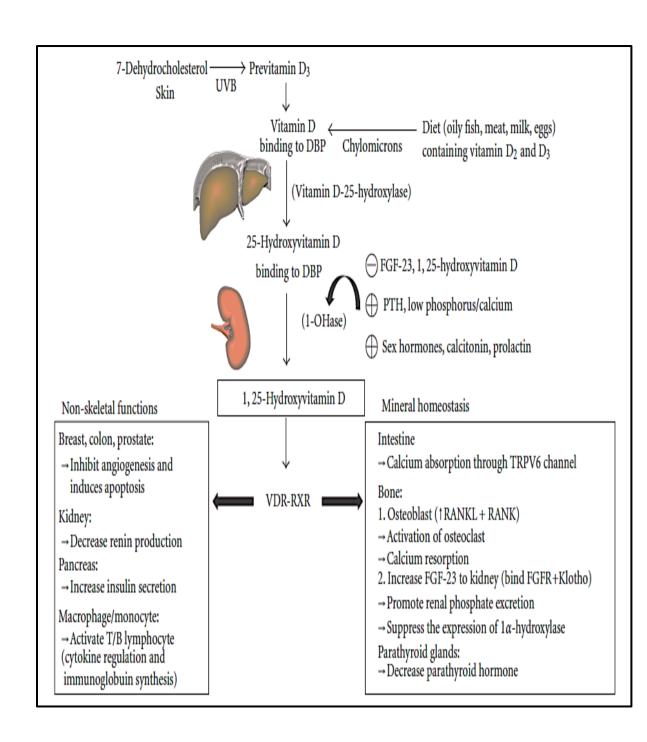
(C28H440) differs from vitamin D3 (C27H440) in the side chain attached to the secosteroid skeleton, which contains an additional methyl group on carbon atom 24 and a double bond between carbon atoms 22 and 23 (*Norman*, 2008).

# Types and sources of vitamin D:

The two main types of vitamin D are: vitamin D3 or cholecalciferol and vitamin D2 or Ergocalciferol. Both types are biologically inactive and must be activated in two metabolic steps before becoming physiologically active (*Taylor et al.*, *2008*) (Diagram II).

After exposure to sunlight or ultraviolet light for 15 minutes for two or three times per week, vitamin D3 is formed in the skin. The ultraviolet (UV) spectrum of sunlight (wave length 290-310 nm) invades the human skin and facilitates the transformation of 7-dehydrocholesterol present in the subcutaneous fat to provitamin D, which undergoes alterations by thermal isomerization to vitamin D3. Restrictions are age, a pigmented skin, sunscreen use, and clothing (*Holick*, 2004).

On the other hand, vitamin D2 can be obtained by irradiation of plants or other types of food (*Feldman et al.*, 2005).



**Diagram II:** Diagram showing sources and functions of vitamin D (*Sung et al, 2012*).

Very few types of natural food contain vitamin D. Fish (e.g., salmon, tuna, and mackerel) and fish liver oils are the greatest sources. Lesser amounts of vitamin D are found in beef liver, cheese, egg yolk, and various types of mushrooms. So vitamin D supplementation is important to maintain sufficient level (*Ovesen et al.*, 2003). Since the amount of vitamin D gained from the diet is often low and limited, many people depend on fortified foods and dietary supplements to get their vitamin D needs during times of insufficient sunlight. Vitamin D3 supplements may be more effective than vitamin D2 supplements at increasing serum levels of 25-hydroxyvitamin D (25(OH) D). This may be because vitamin D3 has a higher affinity for vitamin D-binding protein (*Armas et al.*, 2004).

Moreover, the use of ultraviolet lamps has been suggested. Exposure to UV-B radiation is a simple way to increase the synthesis of 25 (OH) D in the body. There is no risk of intoxication, as any excess of vitamin D3 and provitamin D3 is changed to inert metabolites. The smallest dose of UV-B radiation to the whole body supplies 20,000 IU of vitamin D in a single day (*Audran and Briot*, 2010).