Ain Shams University Girl's College Biochemistry and Nutrition Department

The role of vitamin D_r and calcium in mediating insulin secretion in experimental animals.

Thesis submitted by Dalia Sayed Hanfy Mahmmoud B.Sc. in Biochemistry and Nutrition

In partial fulfillment for Master Degree in Science (M.Sc.) Biochemistry and Nutrition

Supervisors
Prof. Dr. Nagwa Ibrahim Yahia Hassanin
Professor of Nutrition
Biochemistry and Nutrition Department
Girl's College, Ain Shams University

Dr. Hanaa Mostafa Abd El Fattah Lacturer of Biochemistry and Nutrition Girl's College Ain Shams University

Dr. Hanan Mohamed Fathy Abd El Wahab Lecturer of Biochemistry and Nutrition Girl's College, Ain Shams University

Y . . V

To ... My Family

بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا الا ما علمتنا الك انت العليم الحكيم

حدق الله العظيم

(سورة البقرة الاية ٣٢)

جامعة عين شمس كلية البنات قسم الكيمياء الحيوية والتغذية

الدور الوسطي لفيتامين (دم) والكالسيوم في افراز الانسيولين في حيوانات التجارب

رسالة مقدمة من داليا سيد حنفى محمود بكالوريوس في الكيمياء الحيوية والتغذية

كجزء متمم للحصول على درجة الماجيستير في العلوم تخصص الكيمياء الحيوية والتغذية

تحت اشراف أ • د • نجوى ابراهيم يحي حسنين استاذ التغذية بقسم الكيمياء الحيوية والتغذية كلية البنات – جامعة عين شمس

د • هناء مصطفى عبد الفتاح مدرس الكيمياء الحيوية والتغذية كلية البنات – جامعة عين شمس

د • حنان محمد فتحى عبد الوهاب مدرس الكيمياء الحيوية والتغنية كلية البنات – جامعة عين شمس ٢٠٠٧

جامعة عين شمس كلية البنات قسم الكيمياء الحيوية والتغذية

شكر وتقدير

اشكر السادة الاساتذة الذين قاموا بالاشراف وهن : الاستاذة الدكتورة / نجوى أبراهيم يحيى حسنين استاذ التغذية – قسم الكيمياء الحيوية والتغذية كلية البنات – جامعة عين شمس

الدكتورة / مناء مصطفى عبد الفتاح

مدرس الكيمياء الحيوية والتغذية كلية البنات جامعة عين شمس

الدكتورة / حذان محمد فتحى عبد الوماب

مدرس الكيمياء الحيوية والتغذية كلية البنات – جامعة عين شمس

كما اتقدم بالشكر الى كل من قدم لى المساعدة والنصح خلال فترة الدراسة

<u>Acknowledgement</u>

I would like to express my deepest gratitude to prof. Dr. Nagwa Ibrahim Yahia Hassanin, Professor of Nutrition, Biochemistry and Nutrition Department. Girl's college, Ain Shams University, for her valuable advices and helpful guidance during the progress of this thesis also for her keen interest, encouragement and effective guiding during all the stages of the development of the work.

I am greatly honored to express my sincere gratitude to Dr. Hanaa Mostafa Abd El-Fattah and Dr. Hanan Mohamed Fathy Abd El-Wahab, Lecturers of Biochemistry and Nutrition, Biochemistry and Nutrition Department, Girl's college, Ain Shams University for their great help, continuous encouragement throughout the progress of this investigation and advantageous criticism.

Deep thanks and appreciations are offered to my family for their continuous encouragement and help throughout work.

Contents

			Page
	I.	Introduction	١
	II.	Aim of the work	١.
	III	I. Review of Literature	11
	*	The relationship between hypovitaminosis D and diabet	tes
	*	The effect of vitamin Dr and high calcium diet on	
		insulin and glucose responses	
	*	Factors affecting vitamin D metabolism	
	*	The relationship between magnesium and insulin action	l
IV		Materials and Methods	4 4
\mathbf{V}		Results	٣٣
VI		Discussion	٧ ٢
VII	[Summary	۹١
VII	I	Conclusion	97
IX		Reference	٩٧
ΙΙΧ		Arabic summary	

List of Tables

Table (1):	The composition of the basal diet	۲ ٤
Table (^{\dagger}):	The composition of mineral mixture	70
Table $(^{r})$:	The composition of vitamin mixture	77
Table (٤):	Influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium on body weight, feed intake and feed efficiency ratio in experimental rats	٣0
Table (°):	Influence of dietary vitamin D _r deficiency and supplementation with vitamin D _r / high calcium on relative organs weight (g%) in experimental rats	٣٩
Table (ᠳ):	Influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium on serum magnesium (mg / dl), insulin (μu / ml) and fast plasma glucose (mg / dl) in experimental rats	٤٣
Table (^V) :	Influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium on serum calcium (mg/dl) , phosphorus (mg/dl) and alkaline phosphatase (IU/L) in experimental rats	٤٩
Table (^)	Influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium on serum total cholesterol (mg / dl) and triacylglycerols (mg / dl) in experimental rats	0 £

Table (٩)	Influence of dietary vitamin D_{τ} deficiency and supplementation with vitamin D_{τ} / high calcium on serum parathyroid hormone PTH (pg / ml) and thyroxine T_{ϵ} (ng / dl) in experimental rats	01
Table (۱۰):	Influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium on intraperitoneal glucose tolerance test (GTT) in experimental rats	٦٢

	<u>List of figures</u>	-
		Page
Fig. (\):	A representation of the hormonal form of vitamin D functions in the intestine, bone and distal renal tubule to mobilize calcium	۲
Fig. (۲):	Structures of vitamin D metabolism	77
Fig. (*):	Body weight gain (g) in all groups under investigation	٣٦
Fig. (٤):	Feed efficiency ratio in all groups under investigation	٣٧
Fig. (°):	The relative liver weight (gm %) in all groups under investigation	٤٠
Fig. (\(\):	Serum magnesium (mg/dl) in all groups under investigation	٤٤
Fig. (V):	Serum insulin (µu/ml) in all groups under investigation	٤٥
Fig. (^):	Fast plasma glucose (mg/dl) in all groups under investigation	٤٦
Fig. (4):	Serum calcium (mg/dl) in all groups under investigation	٥,
Fig.(\'\'):	Serum Phosphorus (mg/dl) in all groups under investigation	01
Fig.(\\):	Serum activity of alkaline phosphatase (ALP) (IU/L) in all groups under investigation	07

١.

Fig.(\\):	Serum cholesterol (mg/dl) in all groups under investigation	00
Fig.(*):	Serum triacylglycerol levels (mg/dl) in all groups under investigation	٥٦
Fig.(\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	Serum parathyroid hormone levels (PTH) (pg/ml) in all groups under investigation	٥٩
Fig.(\°):	Serum thyroxin levels (T_{ϵ}) (ng/dl) in all groups under investigation	٦٠
Fig (\\\).	Glucose tolerance test	٦٥

List of abbreviation

ALP Alkaline phosphatase.

CaBP Calcium binding protein.

CaR Calcium receptor

DBP Vitamin D binding protein.

FBS Fast blood suger.

FFA Free fatty acid.

GTT Glucose tolerance test.

HP Hypertensive patient .

LPD Low phosphate diet.

LXRs Liver x receptors.

MBI Body mass index.

μ**g** Microgram

ml milli liter

mRNA Messenger ribonucleic acid.

ng Nanogram

NHES National Health and Examination Survey.

NIDDM Non insulin dependent diabetes mellitus.

PTH Parathyroid hormone.

PTX Parathyroidectomy.

RNA Ribonucleic acid.

TYDM Type Y diabetes mellitus.

U.S.A United State of American.

 $UV\beta$ Ultraviolet β radiation .

VDR Vitamin D receptor.

VLDL Very low denisty lipoprotein .

Abstract

The present work was performed to study the influence of dietary vitamin D_r deficiency and supplementation with vitamin D_r / high calcium in mediating insulin secretion in male albino rats .

Sixty five male albino rats (Sprague Dawley Strain) were randomly allocated in groups of thirteen rats each to five diets, which they ate continuously for ¿o days. The groups were put on the following diets throughout the experimental period, (G_1) received the basal diet for r weeks then, received corn oil orally at a dose of of ml / rat three times weekly for \(^{\pi}\) weeks; (G\(^{\pi}\)) received vitamin D\(^{\pi}\) deficient diet containing normal calcium (*, \$ %) and phosphorus (.. " o %) for " weeks then supplemented with oral vitamin Dr at a dose of \ \ug / rat three times weekly for \upsilon weeks; (Gr) received vitamin Dr deficient diet for "weeks then received corn oil orally at a dose of ', oml / rat three times for one week and continued to receive vitamin Dr deficient diet without any supplementation for \forall weeks; (G_{\(\xi\)}) received vitamin Dr deficient diet for r weeks then, received corn oil orally at a dose of ., o ml / rat three times for one week after that, supplemented with oral vitamin Dr at a dose of μg / day / rat for Υ weeks; (G_o) received vitamin D_r deficient diet for "weeks then received corn oil orally at a dose of ., o ml / rat three times for one week after that supplemented with high calcium diet for Y weeks.

Fasting blood samples were taken on the day \mathfrak{so} for the determination of serum magnesium; insulin; calcium;

phosphorus; activity of ALP; total cholesterol; total triacylglycerols; PTH; T: and plasma glucose.

The supplementation with either vitamin Dr or calcium in groups receiving vitamin Dr deficient diet, improved insulin secretion, in addition there were significant increase in the concentrations of serum insulin; magnesium and significant decrease in calcium as will as a alkaline phosphatase (ALP) phosphorus; activity; cholesterol; triacylglycerol; parathyroid hormone (PTH); thyroxine (T₁) and fasting plasma glucose when compared with vitamin Dr deficient group (Gr).

It was concluded that, vitamin D_r or high calcium diet plays a biochemical role in improving glucose clearance and insulin secretion, even the glucose tolerance test, was concluded in G_{ϵ} followed by G_r and finally G_{\circ} .