EFFECTS OF TRAINING PROGRAM ON C-PEPTIDE AS INSULIN PRODUCTIVE MARKER IN OBESE AND NON OBESE MALE ALBINO RATS

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ

أَنْتَ الْعَلِيمُ الْحَكِيمُ

صَدَقَ اللَّهِ الْعَظِيم

البقرة (32)

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LIST OF ABBREVIATIONS

BMI	Body mass index
ECM	Extracellular matrix
GLUT4	Glucose transporter type 4
GLUTs	Glucose transporters
HDL	High density lipoprotein
HSC	Hepatic stellate cells
LDL	Light desity lipoprotein
NAFL	Non alcoholic fatty liver
NASH	Non alcoholic steatohepatitis
NEFA	Nonesterified fatty acid
PC2	Proconvertases
ROS	Reactive oxygen species
STD	Standered deviation
TG	Triglyceride
TMB	Tetramethylbenzidine
TNF-alpha	Tumor necrotic factor –alpha
HSC	Hepato cellular carcinoma
EDTA	Ethylenediaminetetraacetic acid

INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Obesity represents a global epidemic and is a leading cause of illness and death worldwide **(Kopelman, 2000).**

Obesity is associated with countless co-morbidity such as diabetes mellitus, dyslipidemias, cardiovascular diseases and some kinds of cancer, representing hence a huge health problem **(Allison, 2000).**

Changes in the world food economy have contributed to shifting dietary patterns, for example: increased consumption of energy-dense diets high in fat, particularly saturated fat, and low in unrefined carbohydrates. These patterns are combined with a decline in energy expenditure that is associated with a sedentary life style eg: motorized transport **(Kimm, 2002).**

Regular physical exercise offers protection against the development and progress of countless chronic diseases (such as coronary heart diseases, hypertension, obesity and diabetes type two being hence a relevant component of a healthy life style **(Revinter, 2000).**

C-peptide is a protein that is produced in the body along with insulin. First preproinsulin is secreted with an A-chain, C-peptide, a B-chain, and a signal sequence. The signal sequence is cut off, leaving proinsulin. Then the C-peptide is cut off, leaving the A-chain and B-chain to form insulin **(Steiner, 1967).**

C –Peptide serve as an important linker between the A- and the B-chains of insulin and facilitates the efficient assembly, folding, and processing of insulin in the endoplasmic reticulum **(Hills, 2008).**

AIM OF THE WORK

The objective of this study is to determine the effects of muscular exercise training program on c–peptide as insulin productive marker in obese and non obese male albino rats.

REVIEW OF LITERATURE

C-PEPTIDE

Proinsulin C-peptide was first described in 1967 in connection with the discovery of the insulin biosynthesis. It serves as an important linker between the A- and the B- chains of insulin and facilitates the efficient assembly, folding, and processing of insulin in the endoplasmic reticulum **(Steiner, 2004).**

C–peptide was for long considered to be without biological activity of its own **(Al–Rasheed, 2006)**.The great variability of its molecular structure among species and the lack of experimental results supported the general assumptions that it did not have any inherited physiological activity and had no significance beyond being a spacer in the biosynthesis of insulin **(Torn, 2003)**.

But the knowledge that insulin biosynthesis provides the release of equimolar amounts of both insulin and C–peptide into the blood stream has stimulated several authors to look for any significant biological activity related **to C–peptide (Marques et al., 2004).**

Indeed, C–peptide is considered a reliable marker of residual beta–cell function in patients with type 1 diabetes during the long–lasting process of immune destruction of beta–cells, and it may assist in differentiating type 1 from type 2 diabetes **(Chailurkit et al., 2007)**.

In the last number of years, numerous studies in both humans and animals have demonstrated that C–peptide, although not influencing blood sugar control, might play a role in preventing and potentially reversing some of the chronic complications of type 1 diabetes

(Walenciak et al., 2007).

Thus, much more than a byproduct of insulin biosynthesis, C–peptide may also be an active peptide with relevant physiological effects different from and complementary to those of insulin **(Marques et al., 2004)**.

C–peptide was found to have no effect in healthy subjects or animals which suggests the saturation of mechanisms of C–peptide action in healthy subjects **(Tsimaratos, 2004; Forst et al., 2000)**.

What is C peptide?

C-peptide, is a cleavage product of insulin synthesis that is co-secreted with insulin by pancreatic β-cells following glucose stimulation. Equimolar amounts of C-peptide and insulin are stored in secretory granules of the pancreatic beta cells and both are eventually released to the portal circulation. Both are released simultaneously from the pancreas when the compound called proinsulin is split into two pieces. Insulin is responsible for regulating the body's glucose levels. Glucose, the body's main source of energy, is a sugar that comes from foods. After a meal, our bodies break down the foods we eat into glucose and other nutrients, which are then absorbed into the bloodstream from the gastrointestinal tract. Glucose levels in the blood rise after a meal and trigger the pancreas to make insulin and release it into the blood **(Steiner et al., 1969).**

When insulin is released, so is C-peptide. Insulin works like a key that opens the doors to cells and allows the glucose in. Without insulin, glucose can't get into the cells and it stays in the bloodstream. The most common cause of abnormal fluctuations in blood glucose is diabetes. C-peptide, on the other hand, has no effect on blood sugar. It is, however,

useful as a marker of insulin production, since the pancreas typically releases C-peptide and insulin in about equal amounts. In general, high C-peptide levels are associated with increased insulin production, while low C-peptide levels indicate decreased insulin production **(Steiner et al., 1969).**

Recombinant insulin, used in the treatment of diabetes, lacks C-peptide and preclinical and clinical studies suggest that lack of C-peptide may exacerbate diabetes-associated complications. In accordance with this, several studies suggest that C-peptide has beneficial effects in a number of diabetes-associated complications **(Rubenstein et al., 1976).**

C-peptide has been shown to prevent diabetic neuropathy by improving endoneural blood flow, preventing neuronal apoptosis and by preventing axonal swelling **(Kobayashi et al., 2005).**

In the vascular system, C-peptide has been shown to prevent vascular dysfunction in diabetic rats, and to possess anti-proliferative effects on vascular smooth muscle cells, which may prevent atherosclerosis. However, C-peptide depositions have been found in arteriosclerotic lesions of patients with hyperinsulinemic diabetes and C-peptide has been shown to induce pro-inflammatory mediators, such as nuclear factor kappa B, inducible nitric oxide synthase, and cyclooxygenase-2, indicating that C-peptide treatment could be associated with side-effects that may accelerate the development of diabetes-associated complications **(FiorettiI, 1997).**

This clinical observation suggests that there may be other factors that causally contribute to the development of diabetes complications. During insulin biosynthesis, the hormone is synthesized as a single polypeptide,