# Evaluation of the Effect of Heating on Human Subcutaneous Fat In-vitro

Thesis submitted by

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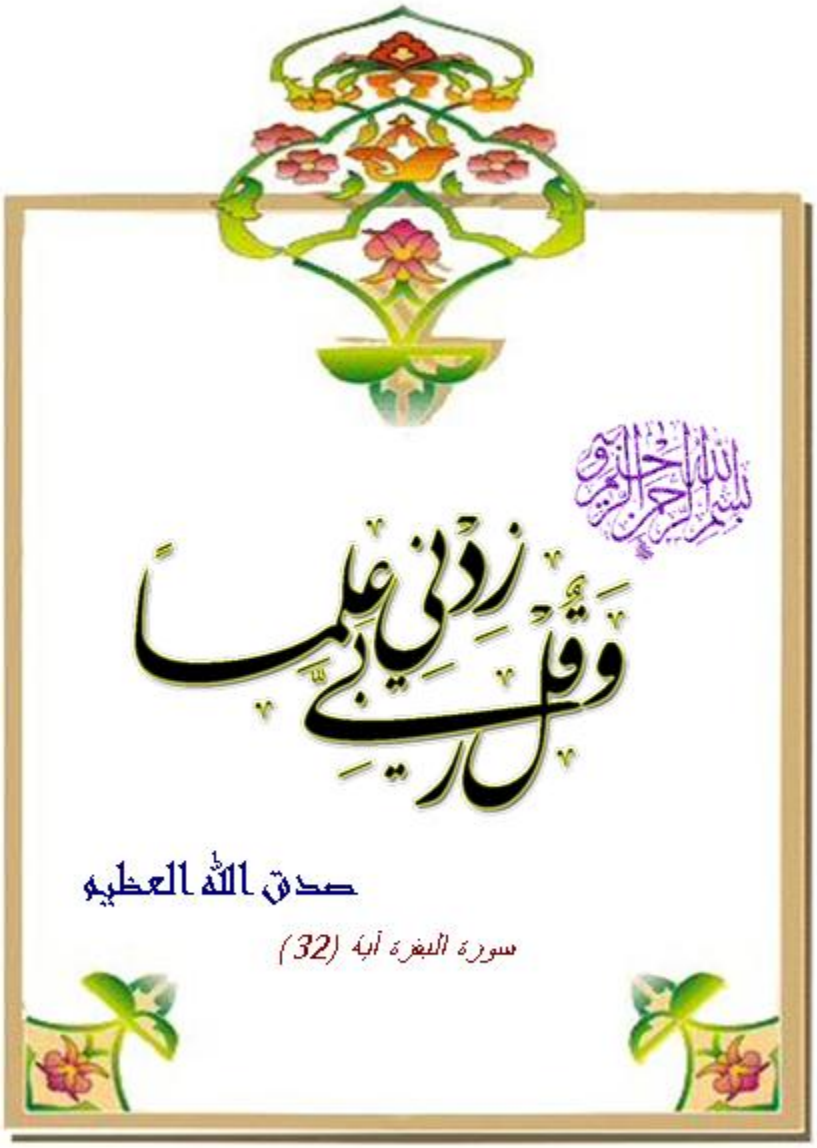
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***Heba Magdy Salleh***

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# *List of Abbreviations*

| | | |
|---|---|---|
| **ATP** | **:** | Adenosine triphosphate. |
| **BMI** | **:** | Body mass index. |
| **cAMP** | **:** | Cyclic adenosine monophosphate. |
| **G proteins** | **:** | GTP binding proteins. |
| **Gi** | **:** | Inhibitory G proteins. |
| **Gs** | **:** | Stimulatory G protein. |
| **GTP** | **:** | Guanosine 5-triphosphate. |
| **HSL** | **:** | Hormone-sensitive lipase. |
| **WAT** | **:** | White adipose tissue. |

# Introduction

Obesity can be defined as an excess of body fat where the size and number of adipocytes or fat cells increases, which typically is associated with considerable health risks ***(Perrone, 2007).***

There are different methods for dealing with excess fat as exercise, dietary manipulation ***(Horowitz, 2003),*** massage, ultrasound waves or pharmacologic treatment whether local (as creams and mesotherapy) ***(Salti et al., 2008)*** or systemic (as fat burners) ***(Schoenfeld., 2004).***

As more women and men want to look and feel better, body contouring and liposculpture continue to grow in popularity ***(DiBernardo et al., 2008)***. The field of nonsurgical lipolysis has grown enormously in the past few years, since several new techniques have been proposed ***(Salti et al., 2008).***

Heat-mediated lipolysis is now reported as an effective method of dealing with excessive subcutaneous fat ***(Wong, 2010***). Laser, light and radiofrequency machines have been developed for the purpose of deep tissue heating with the hope of generating the sufficient temperature at the required depth ***(Wong, 2010).*** In fact, heating to a degree of 45-60$^{o}$c for few minutes has been reported to achieve melting of subcutaneous fat ***(Childs et al.,2009).***

# Aim of The Study

Is to explore in-vitro the exact immediate effect of heating on subcutaneous fat.

# Review Of Literature

## Definition:

Obesity is often defined as a condition of abnormal or excessive fat accumulation in adipose tissue, to the extent that health may be impaired (***Lewell and Flier, 1997).*** Body mass index (BMI), expressed as weight in kilograms divided by height in meters squared ($kg/m^2$), is commonly used to classify excess fat as overweight (BMI 25.0–29.9), obesity (BMI greater than or equal to 30.0), and extreme obesity (BMI greater than or equal to 40.0) ***(Fryar et al., 2012).***

Obesity results from a chronic excess of energy intake over energy expenditure. Total energy expenditure represents the net sum of calories expended to maintain cellular functions (ion gradients, enzymatic reactions, etc), calories expended to perform physical activity, and calories expended in order to modulate energy balance (sometimes referred to as facultative energy expenditure) ***(Lewell and Flier, 1997).***

## Incidence and associated health problems:

Obesity is increasingly being recognized as a major public health problem and has significantly increased among the population over the past 30 years ***(Yosipovitch et al., 2007).*** It affects more than33.0% of population according to 2009–2010 National Health and Nutrition Examination Survey ***(Fryar et al., 2012).***

The abnormal increase in body fat is accompanied by severe health problems resulting in an increased morbidity and mortality. An example of such obesity–related disorders is metabolic

syndrome (obesity, hyperlipidemia, cardiovascular disease, insulin resistance, and type 2 diabetes). Moreover, the risk of other age-related diseases such as cancer and inflammatory disorders also increases with obesity and it is well established that weight loss in obese patients would lead to significant amelioration in these obesity-related disorders ***(Posovszky et al., 2009).***

The mechanisms linking excess fat to metabolic and cardiovascular disorders are not elucidated ***(Björntorp, 1994).*** A common theory is that obesity "especially visceral type" leads to accelerated mobilization of fatty acids into the portal system because of the increased rate of lipolysis in visceral fat cells usually associated with the enlargement of visceral fat depot (mass effect). Elevated portal free fatty acid concentrations can have a number of undesirable effects on the liver functions ***(Frayn et al., 1996).*** Such alteration in liver function may be the cause of glucose intolerance, dyslipidemia, and hyperinsulinemia***(Arner, 1997).***

## Obesity and skin problems:

Obesity is often related to a number of effects on skin physiology, including effects on skin barrier function, sebaceous glands and sebum production, sweat glands, lymphatics, collagen structure and function, wound healing, micro- and macro-circulation, and subcutaneous fat ***(Yosipovitch et al., 2007)***.

Obese individuals demonstrate significantly increased transepidermal water loss and erythema compared with control subjects ***(Loffler et al., 2002)*** and morbidly obese patients usually have dry skin suggesting a fundamentally altered epidermal barrier ***(Yosipovitch et al., 2007)***.

Moreover, obesity is associated with an increased incidence of a number of skin disorders as shown in *table (1)****(Yosipovitch et al., 2007)***.

**Table (1)** Obesity-related skin disorders ***(Yosipovitch et al., 2007)***.

| |
|---|
| Insulin resistance |
| Insulin resistance syndrome |
| Acanthosis nigricans |
| Acrochordons |
| Keratosis pilaris |
| Hyperandrogenism |
| Hirsutism |
| Mechanical |
| Plantar hyperkeratosis |
| Striae distensae |
| Cellulite |
| Adiposis dolorosa |
| Lymphedema |
| Chronic venous insufficiency |
| Infectious |
| Intertrigo |
| Candida |
| Dermatophytes |
| Folliculitis |
| Necrotizing cellulitis/fasciitis |
| Inflammatory |
| Hidradenitis suppurativa |
| Psoriasis |
| Metabolic |
| Tophaceous gout |

## Structure of adipose tissue:

The adipose tissue is a diffuse organ the main function of which is to store energy in the form of triacylglycerol (triglycerides). Fat is stored in special cells (adipocytes) ***(Björntorp, 2000).***

Adipose tissue is comprised of lobules of adipocytes, blood vessels and fibrous septa and is formed of approximately 75-85% lipids and 15 -25% water and proteins ***(Childs et al.,2009).***

The cells of the adipose tissue, the adipocytes, are formed from precursor cells in a multi-step differentiating process ***(Björntorp, 2000).*** Preadipocytes, fibroblast-like cells present in the stromal vascular fraction of adipose tissue, can differentiate to form mature adipocytes and this capacity is present throughout life ***(Frayn et al., 2003).*** With no fat accumulated, an adipocyte would have a diameter of about 10-12 micrometers, about the same size as a lymphocyte. After normal fat accumulation, the diameter increases 10-folds. This means that the volume has increased 1000 folds indicating that adipose tissue has an enormous plasticity and capacity to store depot energy ***(Björntorp, 2000).*** A mature fat cell appearspolyhedral or oval with the nucleus flattened and pushed to the periphery. An adipocyte's mean diameter depends on the volume of accumulated lipid in the adipocyte cells. The volume ratio of lipid to surrounding cytoplasm appears to be so high that the cytoplasm is not visible in some areas ***(Childs et al.,2009).***

Six fatty acids constituted practically all of the fatty acid mixtures in every adipocyte lipid : myristic, palmitic, palmitoleic, stearic, oleic and linoleic. Other acids have been identified, but constitute a very small percentage of all fatty acids within adipocytes. The mean percentage of oleic acid ranged from 47 to

52% depending on anatomical site, age and race. Corresponding ranges for palmitic, linoleic, stearic, palmitoleic, and myristic acids were 22-25%, 11-13%, 4-8%, 4-8%, and 2-3% respectively ***(kokatnur et al.,2011).***

The adipocyte's cytoplasm is separated from the surrounding interstitial spaces by the external lamina, a glycoprotein envelope that superficially resembles the basal lamina of epithelia. In addition, the lipid droplet within the cell is not surrounded by a membrane but its interface with the cytoplasm contains a 5 - 10 nm condensed layer of lipid reinforced by parallel microfilaments 5 nm in diameter ***(Childs et al.,2009).***

Adipocytes are surrounded by a loose network of fine reticular fibers containing collagen fibrils, fibroblasts, lymphoid cells, eosinophils and some mast cells. Adipocytes are well supplied by blood and lymphatic capillaries ***(Childs et al.,2009).***

## Adipose tissue blood flow:

Adipose tissue blood flow after an overnight fast is typically around 3 ml blood per 100 g tissue per minute, whereas in resting skeletal muscle the value is around 1.5 ml blood per 100 g tissue per minute ***(Elia and Kurpad, 1993).*** Subcutaneous abdominal blood flow increases several-folds (up to four folds) in response to a meal ***(Frayn et al 2003).***

## Innervation of adipose tissue:

Besides somatic nerve supply, one obvious signaling pathway relevant to regulation of net fat deposition is the