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Anti-Obesity Effect of Olive Leaves Powder

Done by:

ATHAMNA Fatima

BENOUCHENNE Djamila

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Examination board:

President: Prof. Y. NECIB	Pr. University of Brothers MENTOURI Constantine 1
Supervisor: Dr. A. KHEDARA	M. C. A University of Brothers MENTOURI Constantine 1
Examiner: Dr. T. NOUADRI	M. C. A. University of Brothers MENTOURI Constantine 1

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DEDICATION

I dedicate my dissertation work to my familly and friends.

Special feelings of gratitude to my loving parents, for their continual faithful support during my study.

Thanks and gratitude is also extended, to my sisters Sihem, Mounira, Djohayna, and Rouaida. my uncles Ryad and Hakim, my aunts, Naima, Dalila, Khadra and Alya And my fiance Bilale.

I also pay thankfulness to my best friends; Fatima, Amina, Hadjer, Chayma, Kenza, and Rokia.

Finally, I pray that Allah accept this effort and make it of real benefit to all who read it.

Djamila

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A special feeling of gratitude to my loving parents, to my husband for their continual faithful support during my study.

Thanks and gratitude are also extended, to my sisters Fayza, Naziha, Sonya

And to my brothers: Walid, Abd El wakil, Kamel

I also pay thankfulness to my best friends: Djamila,Imen, Amina, Hadjer, Chayma, Kenza.

Finally, I pray that Allah accept this effort and make it of real benefit to all who read it.

Fatima

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

4-AP: phenol, 4 – aminophenazone

ADP: adenosine-5-diphosphate

AMPK: Adinosine Monophosphat Protein Kinase

AMPK: AMP-activated protein Kinase

ATP: adenosine-5-triphosphate

BMI: Body Mass Index

BP: blood pressure

C: Control

CETP: Cholesteryl Ester Transfer Protein

CHE: Cholestrol esterase

CHOD: Cholesterol oxidase

CNS: Central Nervous System

DAP: dihydroxyacetone phosphate

F&V: Vegetables and Fruits

FFA: Free Fatty Acid

G3P: Glycerol-3-Phosphate

G6PD: Glucose-6-Phosphate Deshydrogenase

GOD: Glucose Oxidase

H_2O_2: Hydrogen peroxide

HDL-C: High Density Lipoprotein

HMPC: Committee on Herbal Medicinal Products

IL-1β: Interleukine-1 β

IL-6: Interleukin-6

IR: Insulin Resistance

LPL: Lipoproteinlipase

MC4R: Melanocortin 4 Receptor

MCF-7: Michigan cancer foundation -7

NEFA: Non Esterified Fatty Acids

OL: Olive Leaves

OLE: Olive Leaves Extract

POD: peroxidase

POMC: Pro-opiomelanocortin

RAS: Renin-Angiotensin System

RBP-4: Retinol Binding Protein-4

SOCS-3: **S**uppressor of Cytokine Signaling

T2DM : Type 2 Diabetes mellitus

TG: Triglycerides

TNFα : Tumor Necrosis Factor α

Var: Variety

VLDL: Very Low Density Lipoprotein

WC: Waist Circumference

WHO: World Health Organisation

ZAG: Zinc-α2-glycoprotein

TABLE OF CONTENTS

Introduction

INTRODUCTION

The olive tree *(Olea europaea, Oleaceae)* is a traditional symbol of abundance, glory, and peace. The olive fruit, its oil, and the leaves of the olive tree have a rich history of nutritional, medicinal, and ceremonial uses **(Sedef *et al.*, 2009)**.

It is native to the Mediterranean and has been known for its medicinal properties since ancient times **(Mosleh *et al*., 2016)**. The olive tree lives and remains productive for thousands of years. It is the first botanical to have documented medicinal use **(Lee-Huang, 2013),** where The first mention of olive leaf's medicinal use in modern times was in 1843 when Daniel Hanbury of England reported a bitter substance from olive leaf tea was the agent responsible for healing malaria and associated fevers **(Silva *et al.*, 2006).**

The olive tree represents for Algeria the most important plant species regarding the area it occupies. Thus, Algeria has 20 million trees spread over an area of 207,822 ha. The mountainous regions of Kabylia are particularly recognized for the culture of the olive trees and the production of olive oil that is the principal fat used in their diets **(Moussaoui *et al*., 2010).**

In recent years, much attention has been focused on using natural products as an alternative therapy for treatment of many diseases (**Zoair, 2014)**, *Olea europaea* leaves have attracted growing interest in the scientific community. Hence, important scientific and technical efforts have been made to determine the value of this agricultural waste **(Nashwa *et al.*, 2014).**

Olive leaves (OL) are a source of many phytochemicals like phenolics and flavonoids compounds (**Yateem, 2014),** that are common plant secondary metabolites which have not only physiological functions in plants but also positive effects for human health because they can act as antioxidant **(Mahmoudi *et al.*, 2015),** anti-diabetic agents (**Al-Okbi *et al*., 2016)**, hypotensive, anti-atherosclerotic **(Haloui *et al.*, 2010),** it is used to enhance the immune system, as an anti-microbial **(Dekanski *et al.*, 2009),** anti-tumor and anti-inflammatory properties **(Haloui *et al.*, 2010).**

Obesity is an energy balance disorder in which energy intake exceeds energy expenditure (**Shen *et al*., 2014)**, resulting in fat accumulation **(Ellulu *et al*., 2014).** That may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems **(Mohamed *et al*., 2014)**. Obesity may cause a plethora of medical conditions such as diabetes (**Luo *et al.*, 2012)**, hypertension, dyslipidemia (**Jensen *et al*., 2013)**, heart disease **(Liao *et al*., 2015).**

Although the association of cardio vascular disease, hypertension, hyperlipidemia and diabetes with obesity suggests a possible role of OL in the regulation of serum lipids and obesity **(Peyrol *et al.*, 2017).** Taking all in consideration, it is of great interest to examine whether OL leads not only to Hypoglycemia but also reduces obesity.

This study was conducted to examine the effect of OL on serum lipids and body fat accumulation in rats. Here we describe that feeding 6.25% Olive leaves powder reduces body fat in rats.

Brief Review On Obesity

1. Brief review on obesity

1.1. Obesity

1.1.1. Definition

Obesity is an energy balance disorder in which energy intake exceeds energy expenditure (**Shen *et al*., 2013)**, resulting in fat accumulation **(Ellulu *et al*., 2014),** that may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems **(Gamal *et al*., 2014)**. It has been recognized as a disease by the World Health Organization (WHO) in 1997, since she became the first non-infectious disease in history. This is an epidemic that affects both industrialized countries those developing countries. It is a public health problem that affects all age groups and all professions (**Karouche *et al*., 2013).**

Obesity is measured through the Body Mass Index (BMI), a simple index of weight–height relationship that indicates amount of body fat used to classify overweight and obesity in adults **(Ellulu *et al*., 2014).**

1.1.2. Epidemiology of obesity

In recent decades the prevalence of obesity and overweight has increased steadily in both developed and developing countries **(Taleb *et al*., 2012).**

Obesity is a complex, multifactorial and largely preventable disease that, along with overweight, affects over one-third of the world's population today. By 2030 an estimated 38 % of the world's adult population will be overweight and another 20 % will be obese **(Hruby, 2014).** It has been estimated that there are approximately **1.9 billion** adults who are either overweight or obese (body mass index, BMI 25 kg/ m2). Among them, over **600 million** are obese (BMI30 kg/m2). According to WHO, this problem of energy imbalance may have contributed to an estimated **3.4 million** death each year including those resulted from cardiovascular disease, type 2 diabetes mellitus, and cancers **(Chang *et al*., 2017).**

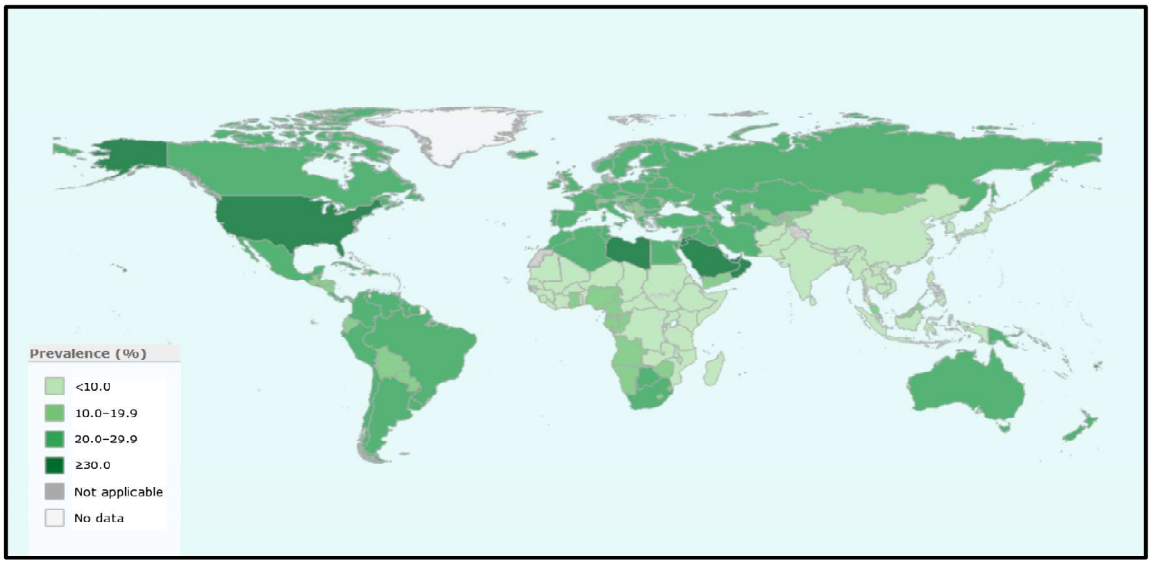


Figure 1: Prevalence of obesity, ages 18+, both sexes, 2014 (age-standardized estimates) source: WHO (**Romieu *et al.*, 2017).**

1.1.3. Classification of obesity

The two most common indexes in classifying obesity are: body mass index (BMI) and waist circumference (**Luo *et al.*, 2012).**

Body Mass Index (BMI)

Body mass index (BMI) is the most widely used method for the diagnosis of obesity and is correlated directly with the risk of comorbidities and mortality **(Liao *et al.*, 2017).** BMI is calculated by dividing a person's weight in kilograms by the square of their height in metres.

Body weight (kg) / height (m) ^{2}

The calculation produces a figure that can be compared to various thresholds showed in **Table 1** for adults that define whether a person is underweight, of normal weight, overweight or obese.

Table 1. Cut points of BMI for the classification of obesity **(Kazan, 2015).**

BMI (kg /m²)	**WHO classification**	**Popular description**
<18 .5	Underweight	Thin
18.5-24.9	Normal range	″Healthy ″, normal or ″acceptable″ weight
25.0-29.9	Grade 1 overweight	Overweight
30.0-39 .9	Grade 2 overweight	Obesity
≥40 .0	Grade 3 overweight	Morbidobesity

Waist circumference

Waist circumference is commonly used as a surrogate measure for abdominal obesity **(Johansson, 2012).** The optimal level for measurement of waist circumference is midway from the lower rib margin to the anterior superior iliac crest, in the standing position.

Table 2. Waist circumference thresholds for abdominal obesity (**Johansson, 2012).**

Sex	Increased risk	High risk
Men	≥ 94 cm	≥ 102 cm
Women	≥ 80 cm	≥ 88 cm

Recent findings have indicated that WC is a stronger marker of health risk than is BMI **(Liao *et al.*, 2017).**

1.1.4. Physiopathology of obesity

Gastric distension via activation of vagal afferents is a signal for satiety, with gastric contractions signalling for hunger. Nutrients, neural impulses and hormones themselves act as afferent signals in the regulation of energy intake and expenditure (**Vassallo, 2007).**Uncontrolled expansion of fat cells leads to obesity and related diseases. The increase in adipocyte number is the result of recruitment of preadipocytes from pluripotent stem cells that reside in the vascular stroma of fat (adipose) tissue. The increase in adipocyte size is the result of increased fat accumulation (**Lee-Huang *et al.*, 2013).**

Fat accounts for 21-37 % of the body weight of middleaged men and women. In case of obese individual more calories are consumed than expended and appetite does not subsequently reduced to compensate for the increase in energy stores (**Panigrahi *et al.*, 2009).** With weight gain over time, excess lipids are distributed to many body compartments. Subcutaneous adipose tissue holds most of the stored lipid at a variety of anatomical sites **(Steven *et al.*, 2017)**. In addition to adipose tissue's main role in releasing fatty acids to be used as energy substrates, this tissue is an active endocrine organ, secreting several hormons and signaling substances with a number of biological functions **(Gambero *et al.*, 2015),** called adipokines (**Kawashima *et al.*, 2017)** such as: leptin, adiponectin, resistin, visfatin, apelin, retinol binding protein-4, vaspin, omentin, ZAG and proinflammatory cytokines (TNFα, IL-6) **(Leal *et al.*, 2013).**

Exemples of adipokines function and obesity

Leptin

Leptin is apeptide hormone produced **(Abdalla, 2017),** by adipocytes **(Vassallo, 2007)**, implicated in the regulation of appetite (**Santi-Cano, 2014).** It acts to reduce food intake and is believed to increase sympathetic nervous system activity **(Vassallo, 2007).**Thus, a deficiency in leptin signaling either via leptin deficiency or leptin resistance leads to overfeeding and may account for some genetic and acquired form obesity**(Gamal *et al.*, 2014)**.

Adiponictin

Adiponectin is the most abundant circulating peptide hormone **(Chun-Laam *et al.*, 2017),** it is almost exclusively synthesized by adipocytes and is present at high levels (3 to 30 μg ml) in the blood.

The beneficial effects of adiponectin on insulin sensitivity seem to be mediated in part by its ability to activate AMP-activated protein kinase (AMPK) in skeletal muscle and liver, because AMPK activation leads to an increase in fatty acid oxidation and glucose uptake in muscle tissue, and inhibition of gluconeogenesis in the liver. Adiponectin expression was found to be decreased in obesity **(Ouchi, 2011)**.

Pro-inflammatory cytokines

Adipose tissue is mainly comprised of adipocytes, although other cell types contribute to its growth and function, including pre-adipocytes, lymphocytes, macrophages, fibroblasts and vascular cells **(Ouchi, 2011).**

Obesity is accompanied by increases in macrophages and other immune cells in adipose tissue, in part because of tissue remodeling in response to adipocyte apoptosis. These immune cells secrete proinflammatory cytokines (TNF***α*)**, which contribute to the insulin resistance that is often present in patients with obesity **(Steven *et al*., 2017)**.

Table3. Adipokines profile in obesity **(Leal *et al.*, 2013).**

Adipokine	**Main function**	**Obesity**
	Energy homeostasis	
Leptin	Benificial: ↑energy expenditure and ↑energy	↑but there is neuronal
ZAG	consumption	resistance to its action
	Benificial : ↑energy expenditure and ↑lipolysis	↓
	Glucose homeostasis	
Adiponectin	Benificial :↑AMPK and ↓gluconeogenesis	↓
Vaspin	Benificial : ↑insulin sensitivity ↓food intake	↑as a compensatory role in metabolic complications
Omentin	Benificial : ↑adipocytes glucose uptake	associated with obesity
Visfatin	Benificial : ↑insulin secretion	↓
		↑but controversial- it is a
Leptin	Harmful : ↑SOCS-3 expression	compensatory response to
Resistin	Harmful : ↑gluconeogenesis and ↓AMPK and	IR
RBP-4	IRS-2	↑
	Harmful : ↑hepatic gluconeogenesis and ↓	↑
TNF-**α**	muscle insulin signaling	↑
IL-6	Harmful : ↓insulin signaling	
	Harmful : ↓insulin signaling	↑
		↑

1.1.5. Risk factors of obesity

Like any other multifactorial diseases, obesity is a complex disease **(Alamukii *et al.*, 2017),** interplaying of both genetic and environmental factors ***(*Perry, 2015).** The causes of obesity are varied and complex **(Scott *et al.*, 2017),** involving social, biological and

psychosocial factors, A sedentary lifestyle and a high-calorie diet seem to be the most important factors in the development of obesity **(Gambero *et al.*, 2015).**

1.1.5.1. Modifiable factors

- **Environment**

factor that has been suggested as being obesogenic is a high energy density of foods (i.e., an energy content of more than about 225–275 kcal per 100 g) (**Romieu et *al.*, 2017),** such as those present in «fast food» **(Rodríguez-Martín *et al.*, 2009),** palatable foods that are often served in large portions; decreasing time spent in occupational physical activities and displacement of leisure-time physical activities with sedentary activities such as television watching and use of electronic devices **(Steven *et al.*, 2017)** such as computer usage, transport mode **(Duncan *et al.*, 2011)**; Medications used for the management of conditions other than obesity can contribute to or exacerbate weight gain in susceptible individuals **(Apovian *et al.*, 2015).**

1.1.5.2.Non modifiable factors :

- **Genetic factors**

Like many other medical conditions, obesity is the result of interplay between genetic and environmental factors. Polymorphisms in various genes controlling appetite and metabolism predispose to obesity when sufficient food energy is present **(Gamal *et al.*, 2014)**.The marked differences in adiposity between individuals seem to be explained mainly by our genes **(Gummesson, 2009)**. Common for most of these genes is their involvement in hypothalamic regulation of food intake, including the leptin gene, the pro-opiomelanocortin (POMC) gene, and the melanocortin 4 receptor gene (MC4R) **(Pepper *et al.*, 2010).** Individuals with mutations in these genes typically present with an increased drive to eat and early-onset obesity **(Gummesson, 2009).**

1.1.6. Consequences and complications associated with obesity

Adipose tissues can influence and communicate with many other organs, including the brain, heart, vasculature, liver and muscle, through the production of various secretory factors or adipokines **(Ouchi *et al.*, 2011).** Obesity is a multifactorial and complex disorder (**Vassallo, 2007),** as a result of dysregulated expression of these factors, caused by excess adiposity and adipocyte dysfunction, has been linked to the pathogenesis of various disease

processes **(Ouchi *et al*., 2011).** It has an adverse effect on health (**Luo *et al.,* 2012)**, that, associated with a shorter life expectancy **(Abdalla, 2017).**

Obesity may cause a plethora of medical conditions such as diabetes (**Luo *et al.,* 2012)**, hypertension, dyslipidemia (**Jensen *et al*., 2013)**, heart disease **(Liao *et al*., 2015).**

1.1.6.1. Diabetes mellitus (T2DM)

In particular, T2DM defined together with obesity (Diabesity) as the XXI Century epidemic **(Liguri *et al.,* 2017).**

Obesity is the main driver for the current epidemic of Type 2 diabetes (T2D). As weight increases, there is increasing insulin resistance. This means that the pancreas has to make more insulin in order to maintain normal blood glucose levels. Fat tissue not only increases the demand for insulin, it also secretes toxins that cause the insulin secreting beta-cells to fail. T2D can occur at any BMI, but there is a sharp increase in risk of T2D when BMI exceeds 30 kg/m^2 **(Price *et al*,. 2015).**

1.1.6.2. Hypertention

Hypertension is probably the most common comorbidity associated with obesity **(Scott *et al.,* 2017).** The renin-angiotensin system (RAS) is well recognized for its key role in regulation of blood pressure, fluid homeostasis, vasoconstriction, hormone secretion, kidney function, and cellular growth Angiotensin is overexpressed in obesity, directly contributing to obesity-related hypertension. This hyperkinetic state is supplanted by increasing evidence of systolic and diastolic myocardial dysfunction, which may progress to overt clinical heart failure **(Rowland, 2007)**.

1.1.6.3. Dyslipidimia

Obesity and dyslipidemia are strongly associated with each other (**Tanveer *et al.,* 2017).** Obesity is the most common cause of dislipidemia **(Gamal *et al*., 2014)**. It is characterized by impaired adipocytes trapping of fatty acids and excessive adipocytes lipolysis. These alterations lead to high circulating non esterified fatty acids (NEFA) levels that result in increased hepatic lipogenesis. Overwhelming of hepatic secretory capacity leads to hepatic steatosis by the newly synthesized triglycerides (TG) and increased VLDL circulating levels. An impaired lipoprotein lipase activity and enhanced cholesteryl ester transfer protein (CETP) - mediated lipid exchanged contribute to the observed HDL-C reduction in obesity (**Santi-Cano, 2014).**

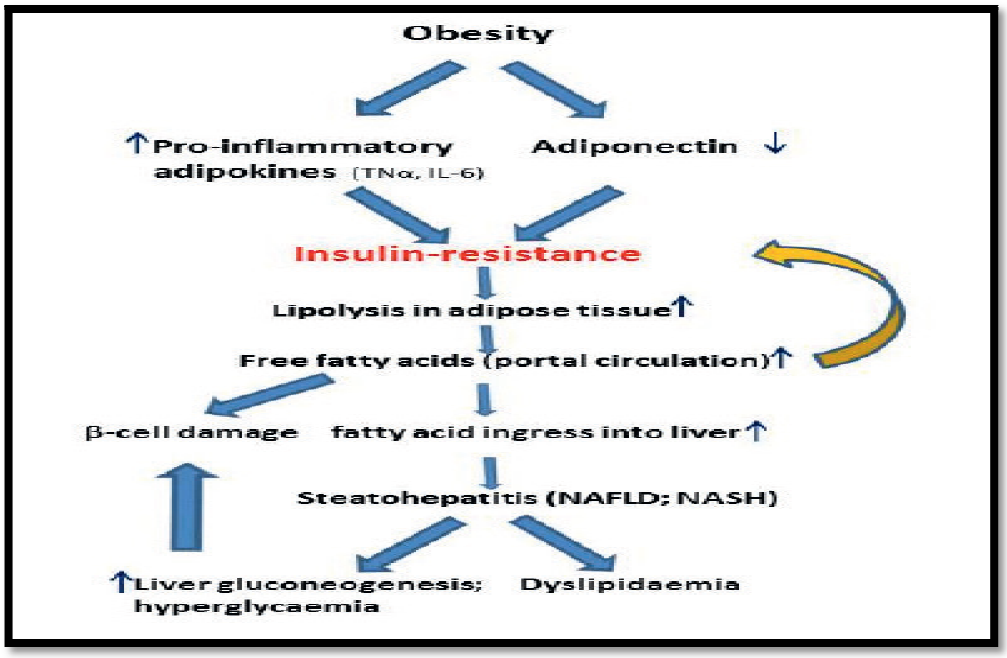


Figure 2. The relationship between obesity and dyslipidemia **(Liguri *et al.*, 2017).**

1.1.6.4. Cardiac alteration

The link between obesity and cardiovascular disease is believed to be through a number of metabolic pathways and their complications such as atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose **(Rowland, 2007).**

1.1.6.5. Cancer

Epidemiological studies have shown that obesity is associated with increased risk of many cancer types **(Xie *et al.*, 2016),** including colorectum, endometrium, kidney, oesophagus, postmenopausal breast, pancreas, gastric cardia, liver, ovary, thyroid, meningioma, multiple myeloma, and advanced prostate cancers **(Romieu *et al.*, 2017).**

The relations between obesity and cancer can be explained by variations in the metabolism of endogenous hormones (contain of insulin, insulin like growth factors and sex steroids) which may cause impairment of the normal balance between cell proliferation differentiation and apoptosis **(Kazan, 2015)**. Secrete multiple biologically active polypeptides that act by endocrine, paracrine, and autocrine mechanisms (**Robert, 2009)**. Different assumed biological mechanisms consisting of changes in the bioavailability and synthesis of sex steroid hormones, insulin resistance, release of growth factors and/or pro-inflammatory cytokines and deviant energy disposal and expenditure can cause progression and genesis of cancer. In addition that, cancer genesis can indirectly be contributed to through a progressive

aggregation of environmental chemical carcinogens in the adipose tissue by a modification of the hormonal milieu **(Kazan, 2015).**

1.1.6.6. Neurological disorders

Psychological damage caused by overweight and obesity ranges from lowered self-esteem to frank clinical depression. Indeed, rates of anxiety and depression are three to four times higher among obese individuals. Obesity significantly increases the risk of Alzheimer's disease. A strong correlation exists between BMI and high levels of amyloid, i.e. the protein that accumulates in the Alzheimer's brain, destroying nerve cells and producing cognitive and behavioral problems **(Gamal *et al*., 2014).**

1.1.7. Management and Treatement of obesity

Obesity is a chronic condition that is difficult to treat (**Gummesson**, **2009)**. The potencies of treatment options for the management of obesity including behavior/lifestyle interventions, pharmacotherapy, and bariatric surgery **(Patel, 2015).**

We recommend that diet, exercise, and behavioral modification be included in all obesity management approaches for body mass index (BMI) 25 kg/m2 and that other tools such as pharmacotherapy (BMI 27 kg/m2 with comorbidity or BMI over 30 kg/m2) and bariatric-surgery (BMI 35 kg/m2 with comorbidity or BMI over 40 kg/m2) be used as adjuncts to behavioral modification **(Apovian *et al*., 2015).**

1.1.7.1. Lifestyle Intervention

Current guidelines suggest the use of comprehensive lifestyle modification as the first-line treatment for obesity. Lifestyle interventions designed to modify eating behaviors and physical activity are the first option for weight management **(Steven, 2017),** Being physically active and following a healthy diet have been shown to reduce the risk of premature death or morbidity **(Kahlert, 2015)**.

1.1.7.2. Pharmacotherapy

Most of the currently available pharmacological treatments of obesity reduce food intake or decrease the efficiency of food absorption in the intestines **(Chabowska-Kita *et al*., 2016).** There are two broad categories into which current anti-obesity agents can be divided. Centrally acting drugs modulate signaling pathways in the central nervous system (CNS) and

thus suppress appetite. Peripherally acting agents promote weight loss by reducing the absorption of nutrients **(Majanović *et al.*, 2016).**

a. apetite Suppressants drugs

a.1. Amphetamines

In the 1940s and 1950s, amphetamines became the primary drugs for obesity treatment. Amphetamines act on hypothalamic receptors to release norepinephrine and, to a lesser extent, dopamine and serotonin, increasing central nervous system (CNS) activity and resting energy expenditure, and decreasing appetite and food intake, thus leading to weight reduction **(Haslam, 2016).**

a.2. Phentermine

Phentermine is a centrally acting sympathomimetic agent, which mainly acts to increase norepinephrine in the CNS, thereby suppressing appetite **(Majanović *et al.*, 2016).**

a.3. Sibutramine

sibutramine acts as a sympathomimetic, blocking neuronal uptake of any released serotonin and norepinephrine, thereby prolonging stimulation of peripheral beta-adrenergic receptors to induce satiety **(Haslam, 2016).**

b. Lipase Inhibitors

b.1. Orlistat

Orlistat is a reversible inhibitor of pancreatic lipase **(Majanović *et al.*, 2016)**, prevent the digestion and absorption of some dietary fats **(Paul *et al.*, 2004)** from the gut. At the standard prescription dose of 120 mg three times daily before meals, orlistat prevents approximately 30% of dietary fat from being absorbed, there by reducing caloric intake **(Majanović *et al.*, 2016).**

1.1.7.3. Bariatric surgery

One of the most successful interventions in extreme obesity is bariatric surgery **(Tehmina *et al.*, 2016)**. Bariatric surgery is indicated in obese subjects who have been unable to lose weight through lifestyle change alone **(Johansson, 2012)**. Bariatric / Metabolic

surgery (BMS) is the only form of treatment for severe obesity that provides significant long-term weight loss and maintenance **(Tehmina *et al.*, 2016).**

Bariatric surgery includes procedures that act by either reducing stomach size or capacity or by passing part of the intestine or a combination of the two. Although the surgical restriction in the size of the stomach was initially assumed to be a major factor in resultant weight loss **(Tehmina *et al*., 2016).**

1.1.7.4. Nutritionnal intervention

- **Vegetables and fruits(**F&V)

Vegetables and fruits are considered in dietary guidance because of their high concentrations of dietary fiber, vitamins, minerals, especially electrolytes; and more recently phytochemicals, especially antioxidants. Interestingly, phytochemicals in F&V have been found to act as anti-obesity agents because they may play a role in suppressing growth of adipose tissue . Adiposity is closely related to biomarkers of oxidative stress and inflammation and a diet rich in F&V can modify these adiposity related metabolic biomarkers in overweight women **(Pem *et al.*, 2015).**

Brief Review on *Olea europeae*

2. Brief review on *Olea europaea* variety: *Chemlali*

2.1. Definition

Olea europaea is a typical fruit-tree widely cultivated in the Mediterranean area, belonging to Oleaceae family, even that its cultivation has been extended to many of the region of the world (**Dekdouk et *al.*, 2015).**

Figure 3. *Olea europaea* tree variety *Chemlali* **(Khedara, Athamna , Benouchenne., 2017)**

2.2. Taxonomical classification of *Olea europaea* var: *Chemlali* (Chiappetta *et al.*, 2012).

Kingdom: *Plantae*

Phylum: *Magnoliophyta*

Class: *Rosopsida*

Order*:* *Lamiales*

Family: *Oleaceae*

Sub-family: *Oleideae*

Genus*:* *Olea*

Species: *europaea*

Variety*:* *Chemlali*

2.3. Botanical description

The olive tree, botanically classified as *Olea europaea* is one of the most important fruit trees **(Afaneh *et al.*, 2015)**. Olive is a shrub with permanent green leaves **(Moghaddam *et al.*, 2013)**, in the family Oleaceae, native to the coastal areas of the Mediterranean region **(Al-Okbi *et al.*, 2016).** The climate is characterized by warm weather and extended sunlight irradiation **(Erbey *et al.*, 2010).** It grows to approximately **6-9** metre in height. Leaves are 7.5 cm long, narrow opposite, lanceolate or linear, with entire margins and acute tips, silver-green (grey green) on top, the underside lighter, containing fine white. The leaves are gathered throughout the year **(HMPC, 2011).**

Figure 4: *Olea europaea* variety *Chemlali* leaves

2.4. Chemical composition of *Olea europaea variety: chemlali*

The chemical composition of olive leaves varies depending on several conditions such as origin**,** proportion of branches on the tree **(Sedif *et al.*, 2009)**, storage conditions, weather conditions, moisture content, and degree of soil contamination **(Vogel *et al.*, 2015).**

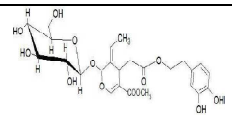
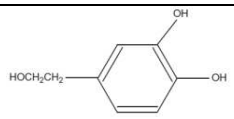
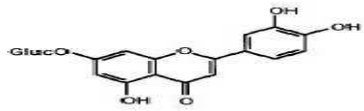
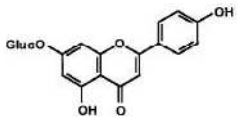
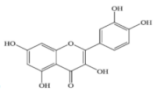
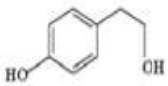
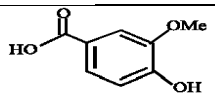
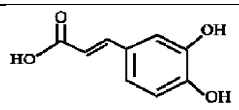
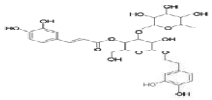
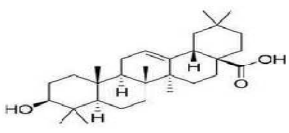
Olive leaves can be considered as a potential source of bioactive compounds. Numerous studies have been focused on the composition of olive leaves based on phenolic compounds considering their richness of such valuable compounds (**Abaza et *al*., 2015).**

- **Phenolic compound**

The olive leaves contain phenolic compounds; the oleuropein, hydroxytyrosol, verbascoside, apigenin- 7-glucoside and luteolin-7-glucoside are the most abundant already identified in olive leaf extracts **(Vogel et *al*., 2015).**

Oleuropein is the major phenolic and the active constituent of olive (*Olea europaea*) leaf **(Al-Azzawie *et al.,* 2006,Afaneh *et al.,* 2015)**, Olive leaves have the highest amount of oleuropein whereas content in olive oil ranges between 0.005% and 0.12% while that in olive leaves ranges between 1% and 14%**.** Studies have shown that oleuropein possesses a wide range of pharmacologic and health promoting properties including, antihyperglycaemic, immune-stimulant, cardioprotective, hypotensive, and anti-inflammatory effects (**Al-Azzawie *et al.,* 2006).**

Table 4. The polyphenol compounds present in olive leaves

Group	**Compound**	**Chemical formula**
secoiroids[1]	Oleuropein[1]	
	Hydroxytyrosol[2]	
Flavonoids [3]	Luteolin-7-O-glucoside	
	Apigenin-7-glucoside[4]	
	Quercitin [5]	
Substituded phenols[6]	Tyrosol [6]	
	Vanilic acid[7]	
	Caffeic acid[7]	
Cinnamic acid derivatives [6]	Verbascoside	
Triterpene[8]	Oleanolic acid	

[1] **Qadir *et al*., 2016;** [2] **Erbay *et al*., 2010;** [3] **Benavente *et al*., 2000;** [4]**Omar, 2010;** [5]**Olayinka *et al*., 2015 ;** [6] **Abaza *et al*., 2015;** [7] **Kawsar *et al*., 2008;** [8] **Alhamd *et al*., 2015.**

- **Fatty acids**

The polyunsaturated fatty acids including the omega-3 and omega-6 families detected in the plants constitute an important class of phytochemicals due to their generalized beneficial health effects **(Guimaraes *et al*., 2009).**

The fatty acid composition of OL is shown in **Table5**. The percentage of polyunsaturated fatty acids in OL of *Chamlali* variety was higher than that of saturated fatty acids and the major fatty acids found were linolenic acid **(Bahloul *et al.*, 2014).**

Table 5. Fatty acids composition in OL of Chamlali variety **(Bahloul *et al*., 2014).**

Fatty acid	Percentage (%)
Linolenic acid (ω_3)	30.02
Oleic acid (ω_9)	26.36
Linoleic acid (ω_6)	14.48
Polyunsaturated fatty acids	44.50
Saturated fatty acids	28.99

- **Fibers**

The greatest proportion of hemicellulose fibers are arabionosa type, whereas the branches have predominantly mannose **(Vogel *et al.*, 2015).**

- **Minerals**

Table7. Mineral composition of olive leaves Variety *Chamlali* **(Bahloul *et al*., 2014).**

Minerals	Amount (mg·g−1 dry matter)
Calcium	10.39
Potassium	7.87
Magnesium	1.50
Sodium	0.82

2.4. Benefits of *Olea europaea L* leaves on human health

Olive leaves have had a lot of medicinal applications in traditional and modern medicine **(Mosleh *et al.*, 2016)**, both the oil and the dried green-grayish colored leaves are used medicinally **(Afaneh *et al.*, 2015).** This plant has been mentioned in traditional medicine as having the following effects **(Moghaddam *et al.*, 2013),** anti-diabetic agents (**Al-Okbi *et***

***al.*, 2016)**, hypotensive, anti-atherosclerotic **(Haloui *et al.*, 2010),** it is used to enhance the immune system, as an anti-microbial and in heart disease **(Dekanski *et al.*, 2009),** anti-tumor and anti-inflammatory properties **(Haloui *et al.*, 2010),** Olive leaf extract was shown to have therapeutic role towards nephrotoxicity, and attenuates obesity in mice **(Shen *et al.*, 2014).**

2.4.1. Anti-oxidant effect

It is known that free radicals cause oxidative stress and therefore they can provoke damaging of DNA molecules, proteins and lipids in biological systems **(Vogel *et al.*, 2014),** leading to different diseases as atherosclerosis, rheumatoid arthritis and inflammatory bowel diseases **(yancheva *et al.*, 2016).** Leaves extract had antioxidant activity higher than vitamin C and vitamin E, due to the synergybetween flavonoids, oleuropeosides and substituted phenols **(Talal *et al.*, 2011).** Many reports indicate that olive leaves contain significant amounts of oleuropein and phenols **(Mourtzinos *et al.*, 2007; Lee *et al.*, 2009; Abaza *et al.*, 2011).** Oleuropein have been reported as a good antioxidant in vitro through chelating of Cu and Fe metallic ions which then catalyse free radical formation and in vivo through the inhibition of enzymatic oxidation such as lipoxygenases (**Qadir *et al*., 2016).**

2.4.2. Anti diabetic effect

Olive-tree leaves are well known as a traditional antidiabetic and antihypertensive herbal drug (**Sedef *et al.*, 2009).** Oleuropein reported to have an antihyperglycaemic effect in diabetic rats **(Al-Azzawie *et al.*, 2006)**. It acts as ROS suppresser and β cell protector in alloxan-induced diabetic rats **(Qadir *et al.*, 2016).** Administration of Olive leaves extract (OLE) reduced significantly the blood glucose levels. Hypoglycemic activity of OLE may result from two mechanisms: increasing peripheral uptake of glucose **(Laaboudi *et al.*, 2016)** and it may also stimulate the release of insulin. Furthermore OLE was found to inhibit the activities of α-amylases from human saliva and pancreas. In Animal models studies the hypoglycemic effect of OLE may be facilitated through the reduction of starch digestion and absorption **(Mousa et *al.*, 2014).** Moreover oleuropein in olive leaves is reported to act as a-glucosidase inhibitor, reducing the absorption of carbohydrates in the gut **(Wainstein *et al.*, 2012)**.

2.4.3. Anti-hypertensive effects

Some indications of olive leaf in traditional medicine are the prevention and treatment of hypertension **(Mosleh *et al.*, 2016)**. The antihypertensive action of olive leaf extract has been shown in several studies **(Vogel *et al.*, 2015).**

The majority of the human evidence involves the use of olive leaf to reduce blood pressure (BP). It has been postulated that oleuropein reduces BP via blockade of L-type calcium channels and verbascoside via inhibition of angiotensin converting enzyme **(MacFarlane, 2016).**

2.4.4. Anti microbial effects

Both Oleuropein and hydroxytyrosol showed antimicrobial activity (*Bacillus subtilis, B. cereus, Staphylococcus aureus, Salmonella typhi, Vibriocholerae, V. parahemolyticus* and *Micrococcussp.*) **(Sabry, 2014)**.The Olive leaves extract inhibitant-viral activities against several types virus like *haemorragic septicaemia rhabdovirus* (**Alhamd *et al.*, 2015).**

OLE may have a role in regulating the composition of the gastric flora by selectively reducing levels of *Helicobacter pylori* and *Campylobacter jejuni* **(Mosleh *et al.*, 2016).**

2.4.5. Cardioprotective effects

The phenolic compounds of olive leaves and olive oils in the Mediterranean diet have been associated with a reduced incidence of heart disease **(Sedef *et al.*, 2009).** Oleuropein, the main constituent of olive leaves extract, protects membrane from lipids oxidation, causes dilatation of coronary blood vessels **(Sabry, 2014)**.

Hydroxytyrosol provides resistance to oxidation, and also it exhibited a range of pharmacological properties beneficial for the cardiovascular system. These actions included enhanced nitric oxide production, decreased blood pressure, inhibition of platelet aggregation **(Satya *et al.*, 2013).**

2.4.6. Effects of olive leaf in chronic colitis

The effect of oleuropein administration in patients with chronic colitis was tested by Giner and collaborators, in a study that evaluated the effects of a diet supplemented with oleuropein, equivalent to 500mg/kg of body weight for 56 days in mice with chronic colitis induced by dextran sulfate sodium **(Vogel *et al.*, 2015).** In the group with the diet supplemented with oleuropein decreased the release of inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-1β (IL-1β). The IL-6 is a pro-inflammatory cytokine that

plays an important role in the development of inflammatory intestinal diseases **(Vogel *et al.*, 2015).**

2.4.7. Anti-cancer effect

Phenolic components, which have a role in cancer prevention are rich in olive leaf (**Mosleh *et al*., 2016)**, among them Oleuropein, which is completely nontoxic in several animal species, has antitumoral activity **(Sedef *et al*., 2009).** Hydroxytyrosol rich extract from olive leaves has *in vitro* anti-tumoral activities and modulates cell cycle progression in MCF-7 human breast cancer cells.Therefore the OLE will be investigated for its probable use as an anticancer food additive (**Mosleh *et al*., 2016)**.

Material And Methods

3. MATERIALS AND METHODS

3.1. Collection and preparation of the plant

Olea europaea leaves (OL), variety: *chemlali* were collected from Agrolival's farm at Wed El Ndjaa, Mila. OL were dried under shade for 13 days then powdered with electric grinder (COBRA, Algeria).

Figure 3. *Olea europaea* tree variety *Chemlali*

Figure 4: *Olea europaea* variety *Chemlali* leaves

3.2. Animals and diets

Males and females *Albinos Wistar* rats, were obtained from animal house (Animal Biology Department, Constantine University 1), weighing 67-236g were used. Rats were individually housed in plastic cages. Room temperature was kept at 24 C° on a 12 h light-dark cycle (lights on, 08:00-20:00 h). All rats were given free access to water and experimental diets. Rats were fed, in a two-ways design, diets with or without containing olive leaves powder (OLP). Composition of the basal diet is listed in Table 1. OLP was added to the basal diet at the level of 6.25%. This level of dietary OLP has been reported that OL has a hypoglycemic effect in diabetic rats **(Moghaddam et *al.*, 2013).** Supplementation of OLP was made at the expense of corn starch. All animals were fed the same amount of experimental diets (12 g d1-5, 14g d6-11, 16g d12, 18g d13 and 20g for d14-35). All the diets were daily incorporated into the food cups in the cages at 11:00h and all rats completely consumed the diets until the next morning. After 5 weeks of consuming diets (5 animals per group), food was removed from the cages at 07:30 h and the rats were anesthetized with chloroform and killed between 11:00 h and 14:00 h. Blood was collected by heart puncture using portal vein prelevement and samples were allowed to clot on ice. Serum samples were obtained by centrifugation (3000 rpm for 20 min). Abdominal adipose tissues (Epididymal and perirenal adipose tissues) and liver were immediately removed, weighed and stored at -20 C˚ until use.

3.3. Experiment

Rats were divided into two groups of 5 rats for each group, control group (C) and olive leaves powder diet group (OLP).

Table 9. Composition of basal diets

	Control group (C)	**Olive leaves powder group (OLP)**
	(% W/W)	
D-Methionine	0.1	0.1
Vitamins mixture[1]	1	1
Salt mixture[1]	3.5	3.5
Casein	20	20
Corn oil	5	5
Sucrose	21.7	21.7
Cellulose powder	5	5
Corn starch	43.5	37.25
Powdered olive leaves	0	**6.25**

[1]Diets are modified version of AIN J. Nutr. 107: 1340-1348 (1977).

3.4. Analytical procedures

Serum concentrations of creatinine and glucose were measured by kits (**CYPRESS DIAGNOSTICS**), Triglycerides are measured by kits (SPINREACT), total cholestrol and albumine were measured using automate (**COBAS *INTEGRA 400 plus***, laboratory of biochemistry, Melitary Hospital, Constantine).

3.4.1. Quantitative determination of Glucose

a. Test principe of Glucose

A colorimetric assay following two coupled enzymatic reactions. A specific enzymatic reaction, in which glucose oxidase (GOD) oxidizes glucose present in the sample to gluconic acid and hydrogen peroxide (H2O2) that serves as the substrate for the peroxidase (POD) in a coupled reaction and it is detected by a chromogenic oxygen acceptor (phenol, 4-aminophenazone (4-AP)) resulting a colored product.

$$\text{Glucose} + O_2 + H_2O \xrightarrow{\text{GOD}} \text{Gluconic acid} + H_2O_2$$

$$H_2O_2 + \text{Phenol} + \text{4-AP} \xrightarrow{\text{POD}} \text{Quinone} + 4H_2O$$

The intensity of the color is proportional to the glucose concentration **(Kaplan *et al.*, 1984)**.

b. Procedure

One milliliter of the reaction mixture containing 92 mM TRIS buffer (pH 7.4), 0.3 mM phenol, 15000 U/L glucose oxidase (GOD), 1000U/L peroxydase (POD) and 2.6 mM 4-aminophenazone (4-AP) was incubated with 10 µl sample. After incubation at 37ºC for 10 Min., optical density of sample and standard (Glucose aqueous primary standard 100 mg/dl) were recorded against blank. At the wavelength 505nm using Spectrophotometer (Ultrospec 2100 *pro*).

The concentration of serum glucose was shown directly on Spectrophotometer's screen.

3.4.2. Quantitative determination of Triglycerides

a.Test principe of Triglycerides

Sample triglycerides incubated with lipoproteinlipase (LPL), liberate glycerol and free fatty acids. Glycerol is converted to glycerol-3-phosphate (G3P) and adenosine-5-diphosphate (ADP) by glycerol kinase and ATP. Glycerol-3-phosphate (G3P) is then converted by (GPO) to dihydroxyacetone phosphate (DAP) and hydrogen peroxide (H_2O_2). In the last reaction, hydrogen peroxide (H_2O_2) reacts with 4-aminophenazone (4-AP) and p-chlorophenol in presence of peroxidase (POD) to give a red colored dye:

$$\text{Triglyceride} + H_2O \xrightarrow{\text{LPL}} \text{Glycerol} + \text{free fatty acids}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{Glycerol kinase}} \text{G3P} + \text{ADP}$$

$$\xrightarrow{\text{GPO}}$$

$$G3P + O_2 \longrightarrow DAP + H_2O_2$$

$$H_2O_2 + 4\text{-AP} + \text{P-Chlorophenol} \xrightarrow{\text{POD}} \text{Quinone} + H_2O$$

The intensity of the color formed is proportional to the triglycerides concentration in the sample **(Buccolo G *et al.*, 1973; Kaplan A *et al.*, 1984)**.

b. Procedure

One milliliter of working reagent contain 50 mM GOOD buffer (pH 6,3), 2 mM p-chlorophenol, 150000 U/L of LPL, 500 U/L of GK, 3500 U/L of GPO, 440 U/L of POD, 0.1 mM 4-AP and 0.1 mM of ATP was incubated with 10 µl sample. After incubation at 37ºC for 5 min, optical density of sample and aqueous primary standard (TRIGLYCERIDE CAL 200mg/dL) were recorded against blank. At the wavelength 505nm using Spectrophotometer (Ultrospec 2100 *pro*).

The concentration of serum triglycerides was calculated by the difference in absorbance between the standard and the sample.

(Abs) Sample / (Abs) Standard * 200 (Standard conc) = mg/dl triglycerides in the sample

Then mg/dl * 0.0113 (conversion factor) = mmol/L.

3.4.3. Quantitative determination of total Cholesterol

a. Test principe of Cholesterol

The cholesterol is determined after enzymatic hydrolysis and oxidation. The quinoneimine indicator is formed by the hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase, according to the following reactions:

$$\text{Cholesterol esters} + H_2O \xrightarrow{\text{CHE}} \text{Cholesterol} + \text{fatty acids}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\text{CHOD}} \text{4-Cholestenona} + H_2O_2$$

$$2\,H_2O_2 + \text{Phenol} + \text{4-AP} \xrightarrow{\text{POD}} \text{Quinonimine} + 4H_2O$$

The intensity of the color formed is proportional to the cholesterol concentration in the sample **(Naito *et al.*, 1984; Meiattini *et al.*, 1978).**

b. **Procedure**

One milliliter of the reaction mixture containing 90 mM PIPES buffer (pH 6.9), 26 mM phenol, 1000 U/L Cholesterol esterase (CHE), 300U/L Cholesterol oxidase (CHOD), 650 U/L Peroxidase (POD) and 0.4 mM 4 – Aminophenazone (4-AP) was incubated with10 µl sample. Each sample had both blank and standard (Cholesterol aqueous primary standard 200 mg/dl). After incubation at 37ºC for 10 min, optical density at the wavelength 505 nm was recorded using Spectrophotometer (MINDRAY. BA-88A). The concentration of serum cholesterol was calculated from the difference in absorbance between the standard and the sample.

(A) Sample / (A) Standard X 200 (Standard conc.) = mg/dl cholesterol in the sample. Then mg/dl X 0.0258 (conversion factor) = mMol/L

3.4.4. Quantitative determination of Albumine

a. Test principe of Albumine

Albumin in the presence of Bromcresol green at a slightly acid pH, produces a colour change of the indicator from yellow-green to green-blue. The intensity of the color formed is proportional to the albumin concentration in the sample.

b. Procedure

One milliliter of the reaction mixture containing 0.12 mM Bromcresol green buffer (pH 4.2) was incubated with 5 µl sample. Each sample had both blank and standard (Albumin aqueous primary standard 5 g/dl). After incubation for 10 min at room temperature (15-25 °C) optical density at the wavelength 630 nm was recorded using Spectrophotometer (MINDRAY. BA-88A). The concentration of serum albumin was calculated from the difference in absorbance between the standard and the sample.

(A)Sample / (A) Standard X 5 (Standard conc.) = g/dl albumin in the sample. Then g/dl X 144.9 = µmol/L.

3.4.5. Quantitative determination of Creatinine

a. Test principe of Creatinine

The assay is based on the reaction of creatinine with sodium picrate, as described by Jaffé. Creatinine reacts with alkaline picrate forming a red complex (Janovsky complex). The

time interval chosen for measurements avoids interferences from other serum constituents (absorbance at 500 nm).

The intensity of the color formed is proportional to the creatinine concentration in the sample **(Kaplan *et al.*, 1984).**

b. Procedure

Creatinine alkaline Reagent containing 0.29 mol/L sodium hydroxide and Creatinine Picrate Reagent containing 25 mM/L picric acid. A working reagent prepared by mixing one volume of creatinine picrate reagent (500µl) and one volume of creatinine alkaline reagent (500µl) directly in spectrophotometer's cuvettes then, 100µl sample was added and mixed well with micropipette.

Analyser calculated automatically serum creatinine concentration.

2.4. Statistical analysis

All results were tested for statistical significance by Student's t-test using StatView softwear.

Results And Discussion

4. Results and discussion

- **The effect of 6.25% of *Olea europaea* leaves powder (*Chemlali*) (OLP) on final and gain body weight**

There was no significant difference on final and gain body weight between the two groups **(Fig 5, 6).** Study by **Shen *et al* (2014)** indicated a trend of lower final and gain body weight in mice by olives extract supplementation to control group for 8 weeks. The no influence of feeding OLP for 5 weeks found in our results, suggesting that the final and gain body weight are mediated through a mechanism involving feeding period and the concentration of the active compounds of OLP.

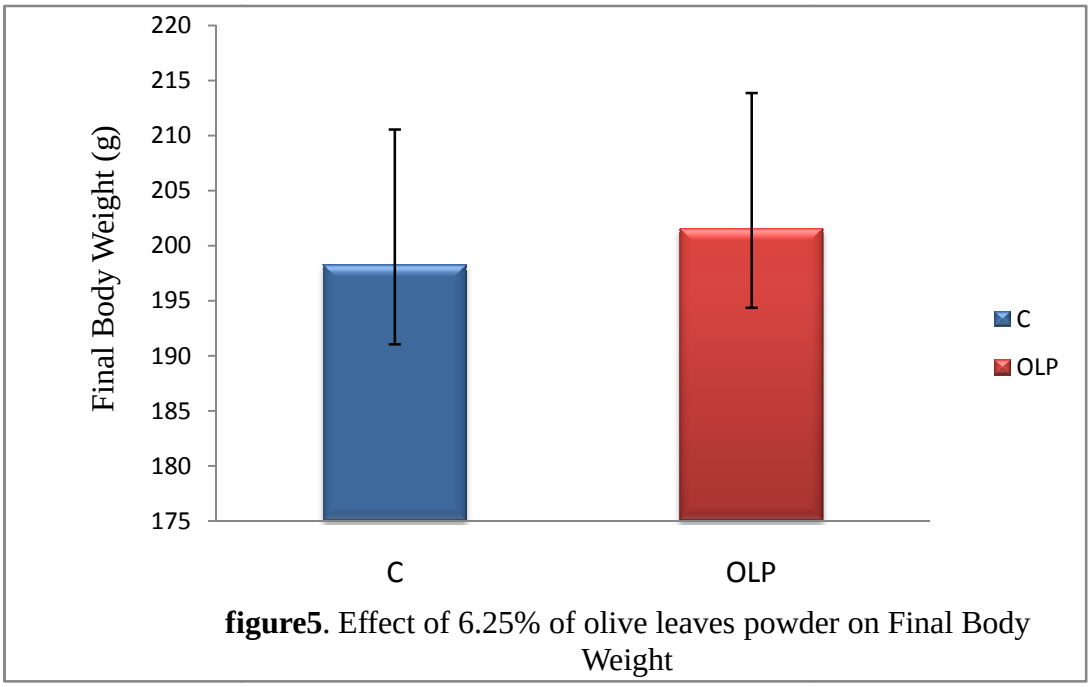


figure5. Effect of 6.25% of olive leaves powder on Final Body Weight

Value are means ± SE (n= 5) for each group

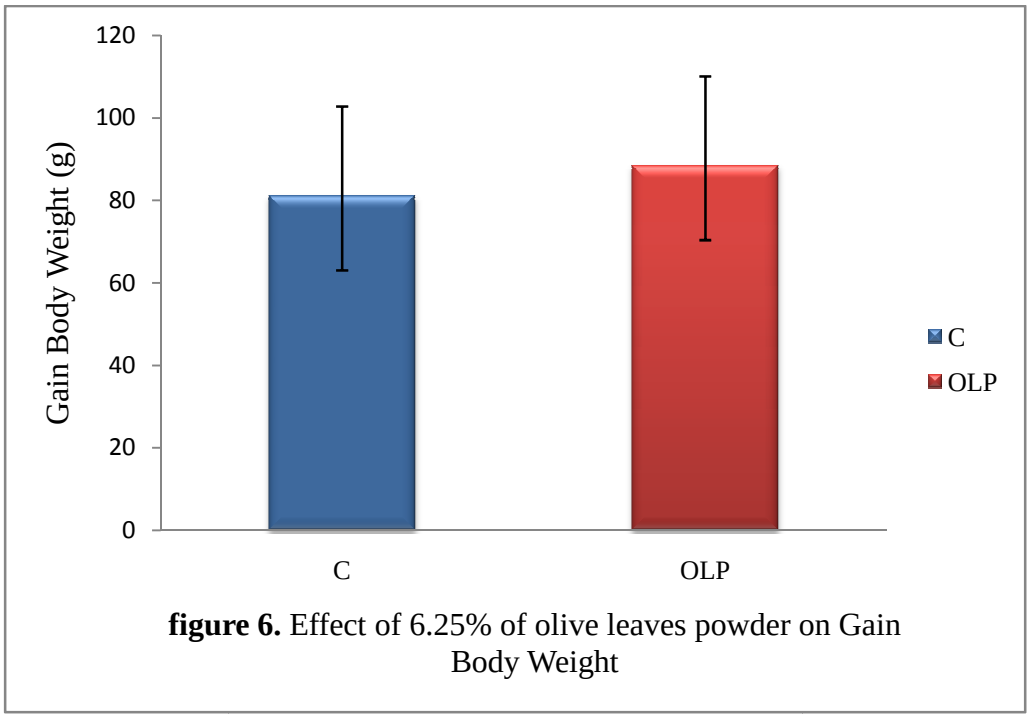


figure 6. Effect of 6.25% of olive leaves powder on Gain Body Weight

Value are means ± SE (n= 5) for each group

- **Effect of 6.25% of OLP on Relative Liver and Kidney Weight**

There was no significant difference in relative liver and kidney weight between the two groups **(Fig 7, 8).**

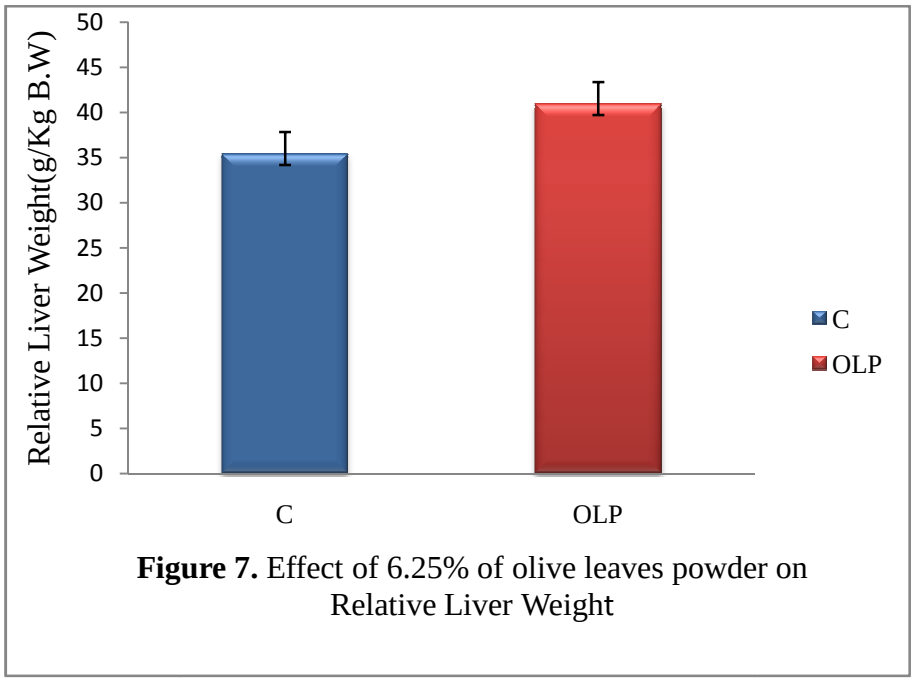


Figure 7. Effect of 6.25% of olive leaves powder on Relative Liver Weight

Value are means ± SE (n= 5) for each group

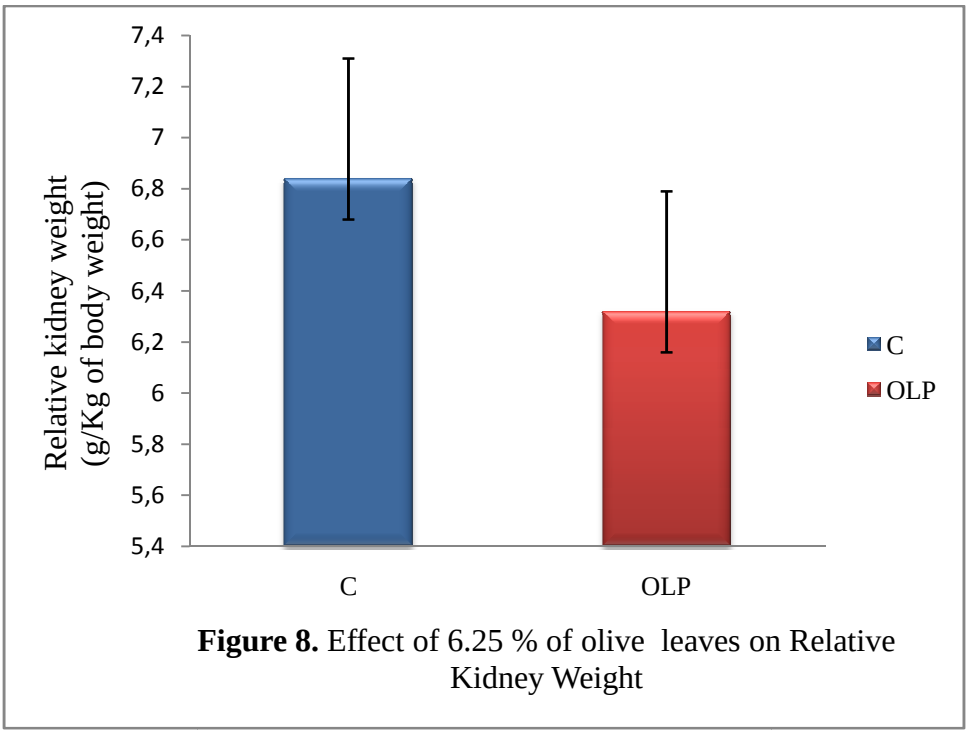


Figure 8. Effect of 6.25 % of olive leaves on Relative Kidney Weight

Value are means ± SE (n= 5) for each group

- **Effect of 6.25% OLP on serum Glucose**

There was no significant difference in serum glucose between the two groups **(Fig 9).** Feeding rats olive leaves extract for 8 weeks significantly lower serum glucose concentration **(Moghaddam *et al.*, 2013; Shen *et al.*, 2014)**.

This difference in our results may be due to the feeding period and the other active compounds present in OLP.

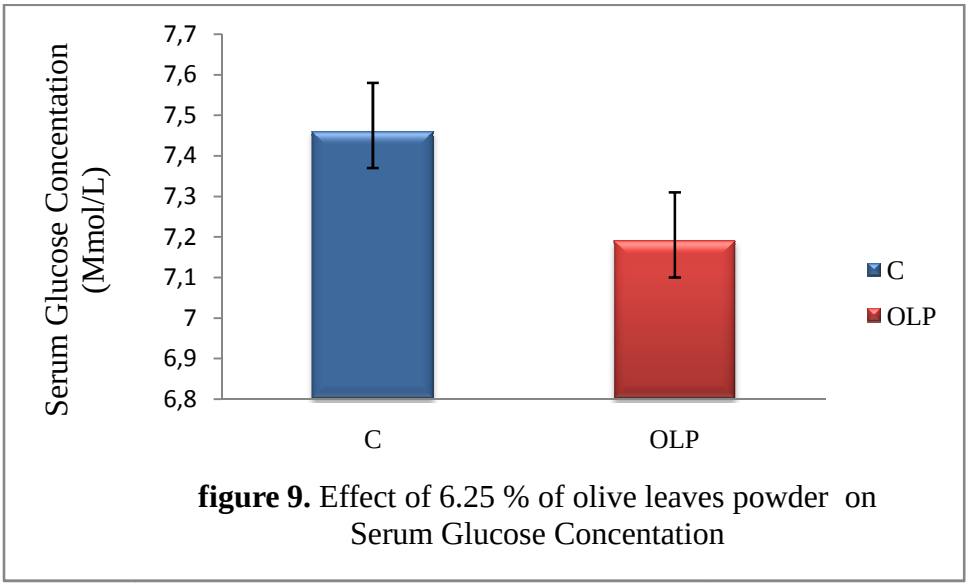


figure 9. Effect of 6.25 % of olive leaves powder on Serum Glucose Concentation

Value are means ± SE (n= 5) for each group

- **Effect of 6.25% OLP on total cholesterol**

There was no significant difference in serum total cholesterol between the two groups **(Fig 10)**. Olive leaves extract is well known to induce hypocholesterolemia **(Moghaddam *et al.*, 2013; Shen *et al.*, 2014; Al-Attar and Shawush, 2014).** The unchanged results found in our study are might due the feeding period and the other active compound in OLP.

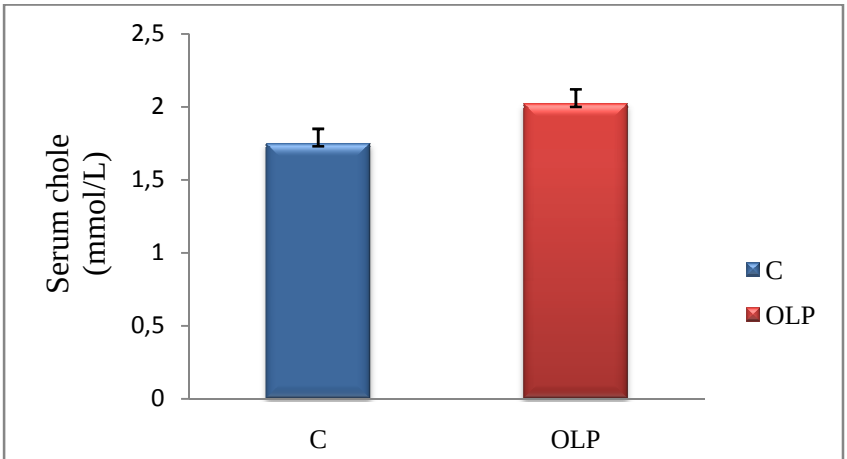


Figure 1O. Effect Of 6.25 % Of Olive Leaves On Seum Cholesterol Concentation

Value are means ± SE (n= 5) for each group

- **Effect of 6.25% OLP on serum Triglycerides**

This study showed that feeding rats **6**.25% of OLP significantly decreased serum TG (32.60%, $P < 0, 05$) **(Fig 11).** Our results are in agreement with the previous studies **(Alzzawi *et al.*, 2004; Moghaddam *et al.*, 2013; Shen *et al.*, 2014)**. The lower concentrations of TG might achieved by two mechanisms either by reducing plasma level of FFA that submitted to beta oxidation, the lower content of FFA, which flows into the liver through, may cause less triglyceride synthesis in the liver **(Shen *et al.*, 2014)** or by augmentation of hydrolysis of TG to FFA by lipase in the liver.

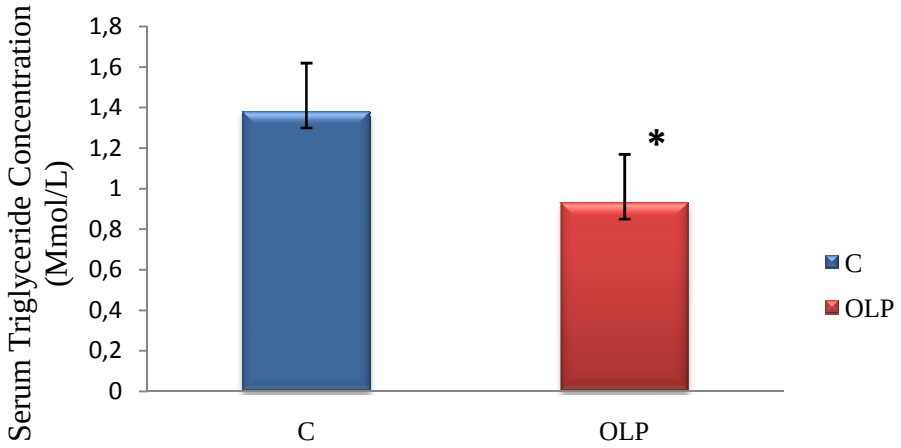


Figure 11. Effect Of 6.25 % Of Olive Leaves Powder Leaves On Serum Triglycerides

Value are means ± SE (n= 5) for each group

*Significantly different from control (*P <0.05).*

- **Effect of 6.25% OLP on Epidydimal and Perirenal adipose tissue weight**

Dietary 6.25% of OLP caused 37% and 45% reduction in epidydimal and perirenal adipose tissue weight respectively **(Fig 22, 13).** Hydroxytyrosol (metabolite of oleuropein) has been known to reduce both of epididymal and perirenal fat formation (**Perol *et al.*, 2017).** In view of this fact, we suggest that the anti-obesity effect of OLP might be at least in part accounted by a common mechanism involving OLP or its compounds as antioxidant nutrients. In consistent with hypotriglyceridemic effect of OLP found in our results, we speculate also that higher fatty acid oxidation due to the activation of carnitine palmitoyltransferase is responsible for the lower accumulation of body weight by OLP. Our results suggest that the anti-obesity effect of OLP is mediated through oleuropein by a mechanism involving higher fatty acids oxidation. Further study is needed to explain the phenomena by measuring serum free fatty acid and the activity of carnitine palmitoyltransferase as a rate limiting enzyme of mitochondrial fatty acid oxidation and also the activities of enzymes of lipogenesis such as G6PD and FAS.

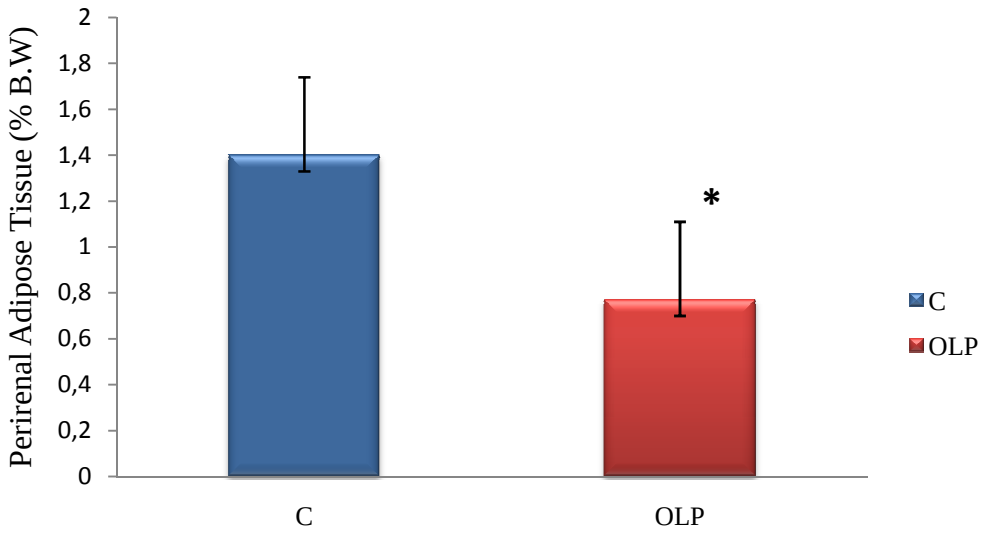


Figure 12. Effect of 6.25% of olive leaves powder on Perirenal Adipose Tissue

Value are means ± SE (n= 5) for each group

*Significantly different from control ($P < 0.05$).

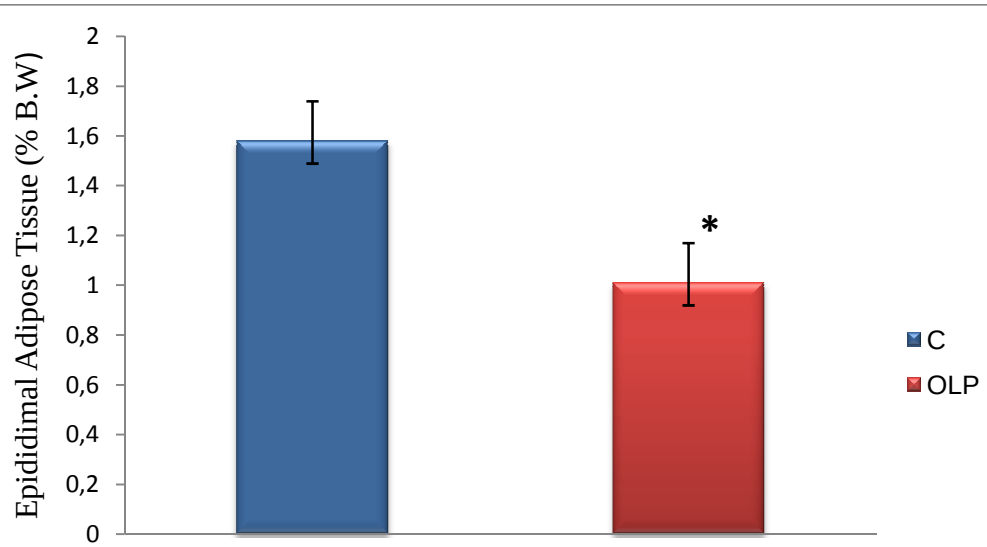


Figure13. Effect of 6.25% of olive leaves powder on Epididimal Adipose Tissue

Value are means ± SE (n= 5) for each group

*Significantly different from control ($P < 0.05$).

- **Effect of 6.25% *OLP (Chemlali)* on serum Albumine and creatinine**

Dietary addition of 6.25% of OLP significantly caused elevation of serum creatinine and slightly lowered serum albumine **(Fig 14, 15).** The same results were obtained with supplementation of olive leaves extract (**Al-janabi *et al*., 2015**).

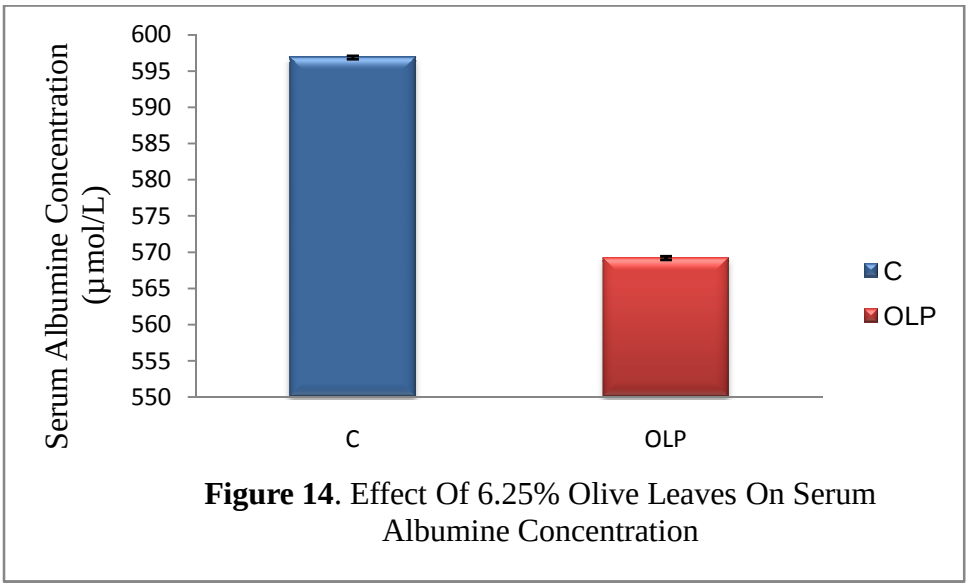


Figure 14. Effect Of 6.25% Olive Leaves On Serum Albumine Concentration

Value are means ± SE (n= 5) for each group

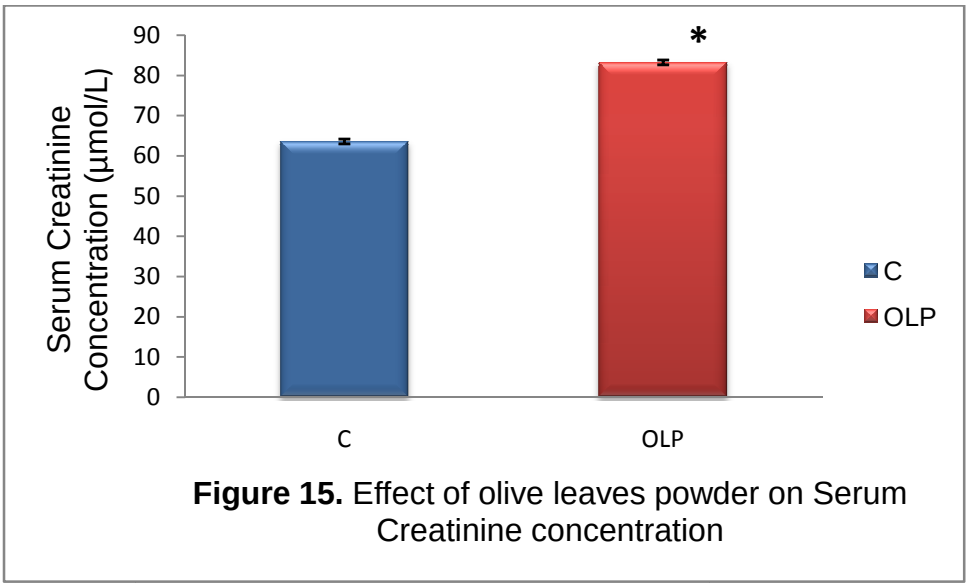


Figure 15. Effect of olive leaves powder on Serum Creatinine concentration

Value are means ± SE (n= 5) for each group

*Significantly different from control ($P < 0.05$).

Conclusion

CONCLUSION

Obesity is a chronic disease of multifactorial origin that develops from the interaction of lifestyle and genetic factors.

Obesity is not only considered as a disease in itself, but it also gives rise to and aggravates many others, and is thus known to be a risk factor for certain chronic diseases, in particular being closely associated with pathologies like diabetes, cardiovascular diseases, osteoporosis and certain types of cancer **(Rodríguez-Martín, 2009).**

Evidences are emerging to support that an increasing consumption of herbs are effective strategy for obesity control and weight management. For centuries people across the countries have been using natural products as plant based dietary supplements for weight control **(Sekaran *et al.*, 2012).**

It was known that OLE has hypotensive, anti-diabetic and anti-cancer effect that due to its richness by polyphenols and this study provided that feeding 6.25% of OLP significantly decreased serum triglycerides level, visceral fat-pad weights, our study demonstrated that supplementation with OLP is helpful to combat or prevent obesity. The anti-obesity effect was demonstrated by hypotriglyceridemia through a mechanism involving activation of fatty acids oxidation as result reduction of body fat accumulation. Further, this study is needed to measure serum free fatty acid, the activity of lipase, hepatic carnitine palmitoyl transferase (CPT), as a key enzyme of mitochondrial fatty acids oxidation and also the activities of enzymes of lipogenesis such as G6PD and FAS.

In summary, this study showed that consumption of OLP reduces serum triglycerides and abdominal adipose tissues weight (epididimal and perirenal). So, OLP have an anti-obesity effect.

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Abstract:

Olive tree *(Olea europaea)* is one of the most important fruit trees in Mediterranean countries. In Algeria, olive tree is one of the most important tree cultivated, whereas variety of *Chamlali* is the most spread wideolive tree. Olive leaves (OL) have the highest antioxidant among the different others parts of olive tree. OL have been used in traditional medicine to lower hypertension and diabetes and both of diseases are associated with obesity.

This study aimed to examine the effect of dietary addition of 6.25% of *Olea europaea* leaves variety *chamlali* powder (OLP) on serum lipids level and fat accumulation. Rats were fed for 5 weeks diets with or without 6.25% of OLP.

Supplemented diet with 6.25% of OLP caused reduction of 37%, 45% in relative epididymal and perirenal adipose tissue weight respectively. OLP also caused 32.60% decreasing in serum triglyceride concentration.

This study showed that 6.25% of OLP have an anti-obesity effect by reducing fat accumulation through a mechanism involving its active compounds such as oleuropein

Keywords: *Olea europaea* leaves, hypotriglyceridemia, adipose tussue, obesity.

Résumé:

L’Olivier (*Olea europaea)* est l’un des arbres fruitiers les plus importants dans les pays méditerranéens. En Algérie, l'olivier est l’un des arbre les plus cultivés et les plus important, dont la variété de Chamlali est la variété la plus repartie. Les feuilles d’olives ont la quantité des antioxydants la plus élevée parmi les différentes autres parties d'olivier. Les feuilles d’olive ont été utilisé dans la médecine traditionnelle pour baisser l'hypertension et attenue le diabète et les deux maladies associées avec l'obésité.

Cette étude a eu pour but d'examiner l'effet de régime alimentaire 6.25 % de la poudre des feuilles *d'Olea europaea*la variété *Chamlali* sur le niveau de lipides sériques et l'accumulation des grasses. Les rats ont été alimentés pour régimes pendant 5 semaines avec ou sans 6.25 % de la poudre des feuilles d'olive.

Le régime Complété avec 6.25 % de la poudre des feuilles d'olive a causé la réduction de 37 %, 45 % dans le poids du tissuea dipeau épididymairerelatif et le poids du tissue adipeux péricardiaque respectivement, les feuilles d’olives provoquent aussi une diminution de

32.60 % dans la concentration sérique de triglycérides.

Cette étude a montré que 6.25 % de la poudre des feuilles d’olive pourraient être ont un effet d'anti-obésité en réduisant l'accumulation des grasses par un mécanisme impliquant ses composés actifs comme oleuropeine ou d’autres composés comme les fibres.

Mots-clés: les feuilles d’*Olea europaea*, hypotriglyceridemia, tissue adipeu, obésité.

ملخص:

شجرة الزيتون من أهم و اغلب الاشجارالمزروعة في بلدان البحر الابيض المتوسط. يعد نوع الشملالي من انواع اشجارالزيتون الاكثر انتشارا في الجزائر, تعتبر اوراق الزيتون الاغنى من حيث مضادات الاكسدة مقارنة بالاجزاء الاخرى لشجرة الزيتون و هذا لوفرة المركبات الفينولية بها.تستعمل اوراق الزيتون في الطب التقليدي لعلاج ارتفاع ضغط الدم و داء السكري, كل من هذه الامراض تعتبر من خلفيات مرض السمنة.

لذا هذه الدراسة تهدف لفحص تاثير 6.25 % من مسحوق اوراق الزيتون على نسبة الدهون في الدم و تراكم الدهون في الجسم. تم علف الجردان بغذاء مع او بدون مسحوق اوراق الزيتون لمدة خمسة اسابيع.

إضافة 6.25 % من مسحوق اوراق الزيتون لغذاء الجردان ادى الى تخفيض الوزن النسبي للنسيج الدهني البربخي بنسبة 37%, و النسيج الدهني المحيط بالكلى بنسبة 45 %, و تخفيض تركيز الغليسريدات الثلاثية بنسبة 32.60%.

هذه الدراسة أظهرت أن 6.25 % من مسحوق اوراق الزيتون له تاثير مضاد للسمنة وذلك بخفض الغليسريدات الثلاثية تراكم الدهون من خلال الية تقحم المركب الاساسي في أوراق الزيتون.

الكلمات المفتاحية : أوراق الزيتون , الغليسريدات الثلاثية, النسيج الدهني, السمنة

Academic year : 2016-2017 **Done by : ATHAMNA FATIMA**

BENOUCHENNE DJAMILA

Dissertation to get Diploma of Master in
Molecular Nutrition and Health

Anti-obesity Effect of Olive Leaves Powder

Abstract:

Olive tree *(Olea europaea)* is one of the most important fruit trees in Mediterranean countries. In Algeria, olive tree is one of the most important tree cultivated, whereas variety of *Chamlali* is the most spread wide olive tree. Olive leaves (OL) have the highest antioxidant among the different others parts of olive tree. OL have been used in traditional medicine to lower hypertension and diabetes and both of diseases are associated with obesity.

This study aimed to examine the effect of dietary addition of 6.25% of *Olea europaea* leaves variety *chamlali* powder (OLP) on serum lipids level and fat accumulation. Rats were fed for 5 weeks diets with or without 6.25% of OLP.

Supplemented diet with 6.25% of OLP caused reduction of 37%, 45% in relative epididymal and perirenal adipose tissue weight respectively. OLP also caused 32.60% decreasing in serum triglyceride concentration.

This study showed that 6.25% of OLP have an anti-obesity effect by reducing fat accumulation through a mechanism involving its active compounds such as oleuropein.

Keywords: *Olea europaea*, hypotriglyceridemia, adipose tissue, obesity.

Reaserch Laboratory: Biochimestry Laboratory, Military Hospital. Constantine

Examination Board:

President: Dr. Y. NECIB	Pr. University of Brothers MENTOURI Constantine 1
Supervisor: Dr. A. KHEDARA	M. C. A University of Brothers MENTOURI Constantine1
Examiner: Dr. T. NOUADRI	M. C. A University of Brothers MENTOURI Constantine1

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