

## Potential Effects of Resveratrol on Obesity Markers of Iraqi Women

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### Abstract

Obesity is defined as a condition of chronic oxidative stress and chronic systemic inflammation, and it is associated with many health problems. Resveratrol is a polyphenolic compound noted to exert beneficial effects on various diseases such as cardiovascular diseases, atherosclerosis, diabetes mellitus, and nephropathy. The healthful effects of resveratrol are thought to be attributed to its antioxidant properties. In this interventional prospective randomized controlled trial, female patients diagnosed with obesity according to the WHO criteria and were randomly allocated to either control or resveratrol group. Resveratrol supplement showed a significant reduction in weight, body mass index (BMI) and waist circumference (WC). From the above results, one can conclude that oral supplementation of resveratrol can improve Anthropometric parameters.

**Keywords:** obesity, resveratrol, body mass index.

### Introduction

Obesity is defined as a global health problem in which excess body fat has accumulated to the extent that it may have a harmful effect on the health<sup>(1)</sup>. People are classified obese when their body mass index (BMI), a value obtained by dividing a person's weight by the square of the person's height, is over 30 Kg/m<sup>2</sup> with the range of 25-30 Kg/m<sup>2</sup> considered as overweight<sup>(2)</sup>. There is a strong relationship between obesity and a variety of diseases, including hypertension, diabetes mellitus, hyperlipidemia, osteoarthritis, cancer, and nephropathy<sup>(3)</sup>. It is recognized that abdominal obesity (android obesity or central obesity) is associated with increased risk of cardiovascular disease (CVD) and type 2 diabetes, whereas gynoid obesity (lower body obesity characterized by fat located around the hips and buttocks) is rarely correlated with metabolic complications<sup>(4)</sup>. Both increased food intake and the lack of physical activity are believed to explain most cases of obesity. In addition, other factors including genetics, medical conditions, lack of sleep and use of drugs, all can predispose to obesity<sup>(5)</sup>. Dietary changes and exercise represent the first step in the management of obesity, Low calorie and fibers rich food such as fruits, vegetables are good food to have every day. In addition to dietary changes, moderate intensive activity of 150 to 250 minutes every week is helpful to lose weight<sup>(6)</sup>.

Resveratrol (3,4,5-trihydroxy-trans-stilbene) is a natural non - flavonoid polyphenolic compound found in Grapes, red wine, Polygonum cupsidatum roots, peanuts, and berries of Vaccinum species, that has many healthful effects including cardioprotective, neuroprotective, antitumor and nephroprotective properties<sup>(7)</sup>. The basic structure of resveratrol consists of two phenolic rings linked to each other by a double styrene bond, and this double bond is responsible for the isometric cis-and trans-forms of resveratrol<sup>(8)</sup>. The major metabolites of resveratrol are the glucuronide- and sulfate-conjugates, where the glucuronide conjugates are documented to be the major metabolites in the rodents, while sulfates are primarily found in humans<sup>(9)</sup>. The main resveratrol target is the sirtuin class of nicotinamide adenine dinucleotide (NAD)-dependent deacetylases. There are seven sirtuins have been exhibited in mammals, of which SIRT-1 is thought to be responsible for the beneficial effects of resveratrol. The pathways that are regulated by sirtuins include fat metabolism, gluconeogenesis and glycolysis in the liver and cell survival<sup>(10)</sup>.

### Patients and Method

This interventional prospective randomized controlled trial was carried out on 50 female patients diagnosed with obesity according to the WHO criteria, with BMI  $\geq 30$  kg/m<sup>2</sup>, age range of 20-50 years old, and waist circumference of  $> 80$  cm, under supervision of professional endocrinologists, from August 2019 to November 2019. The protocol was reviewed and approved by the Scientific and Ethics Committee in the College of Pharmacy/ University of Al-Mustansiriayah, and Obesity Research and Therapy Unit in Alkindi College of Medicine/ University of Baghdad. Patient's oral consent was taken and all participants were advised to take a low carbohydrate and fat dietary regimen and achieving 60 minutes of aerobic exercise per day during their treatment duration. Certain exclusion criteria were followed to avoid interference with the study design and include: Uncontrolled thyroid function, pregnancy and lactation, those on vitamins or dietary supplements, patients with a history of resveratrol allergy, patients on medications that may interfere with resveratrol absorption, patients on drug therapy that may increase body weight, like oral contraceptives.

Female patients were randomly allocated to either control group (taking orlistat) or resveratrol group (taking orlistat plus resveratrol). From 50 female patients, only 46 completed this study, the other 4 were excluded (3 from control group and 1 from resveratrol group) due to poor compliance, violation of the study protocol, or other reasons. At baseline and for all patients, a specially designed questionnaire was filled, recording their medical history and pretreatment characteristics. The demographic and baseline characteristics were evenly distributed for both groups, as summarized in table 1. Parameters of the anthropometry, were evaluated at baseline (pre-treatment) and after 8 weeks (post-treatment) for both groups. Adverse effects (if any) recorded at the end of study.

**Table 1:** Baseline characteristics for control and resveratrol groups

Baseline characteristics	Control group (n=22)	Resveratrol group (n=24)	P-value
Age (years)	37.25±5.557	37.35±6.697	0.895
Weight(kg)	108.05±10.417	108.7±13.031	0.821
Height (cm)	158.63±5.633	158.72±6.531	0.987
BMI (kg/m <sup>2</sup> )	42.635±3.402	42.854±3.655	0.861
Waist circumference(cm)	121.52±8.099	121.34±12.791	0.886

Duration of obesity	11.241±2.132	11.357±3.2	0.876
Data were expressed as mean ± standard error of mean (SEM) or percentage %, BMI=body mass index, N = no. of patients, P- value > 0.05 considered not significant difference.			

### Statistical analysis

The results were presented as mean ± SEM or percentage of difference. All of the statistical analyses were achieved via the statistical package SPSS version 22.0 (SPSS, Inc.). Two sample t-test was applied to compare the means of the baseline characteristics between the two groups and then data were analyzed by using the analysis of covariance (ANCOVA) for this clinical trial. The significance level for all tests was taken as P-value less than 0.05.

### Results

After adjustment of baseline means for control and resveratrol groups according to the analysis of covariance, there was a significant reduction (P-value <0.05) in anthropometric parameters (weight, body mass index and waist circumference) in resveratrol group compared with control group (table 2).

**Table 2:** Effect of resveratrol supplement on anthropometric parameters.

Parameter	Group	Adjusted baseline mean	Adjusted endline mean±SEM	Outcome mean±SEM	P-value	% of difference
wt (kg)	Control N= 22	108.46	105.39±0.665	-3.07±0.665	0.021	↓2.84%
	Resveratrol N= 24		96.35±0.637	-12.11±0.637		↓11.16%
BMI (kg/m <sup>2</sup> )	Control N= 22	42.65	41.42±0.282	-1.23±0.282	0.001	↓2.88%
	Resveratrol N= 24		38.353±0.270	-4.297±0.270		↓10.07%
W.C (cm)	Control N= 22	121.3	118.12±0.734	-3.18±0.734	0.001	↓2.62%
	Resveratrol N= 24		112.89±0.703	-8.41±0.703		↓6.93%
Data expressed by mean ±SEM and percentage of difference P<0.05 was considered a significant difference between treatment groups at end line N= number of patients, SEM = standard error of mean, wt = weight, BMI = body mass index, W.C =waist circumference.						

### Discussion

The present study indicated that the patients on resveratrol supplement in a dose of 1000 mg twice a day for 8 weeks showed a significant reduction (p<0.05) in weight, BMI, and waist circumference (11.16%, 10.07% and 6.93%, respectively) compared with those on control for the same period of treatment (2.84%, 2.88% and 2.62%, respectively) and this agree with Mendez del Villar *et al.* study that showed a significant reduction in weight, BMI and waist circumference after using resveratrol at a dose of 500mg for 90 days<sup>(11)</sup>. Poulsen M. M. *et al.* showed that treatment with resveratrol supplementation had no effect on energy expenditure, adipose tissue content and metabolic events<sup>(12)</sup>. Mechanisms contributing to anti-obesity effects of resveratrol are inhibition of adipogenesis and lipogenesis. The inhibition of adipogenesis and lipogenesis was partially mediated by suppression of insulin signaling and activation of AMP-activated protein kinase (AMPK) α1<sup>(13)</sup>. Lipolysis is another mechanism by

which resveratrol inhibit obesity. The breakdown of triacylglycerol in adipocytes to release free fatty acids and glycerol is regulated by two major enzymes: adipose triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL). Resveratrol has promoted lipolysis, mainly through enhancing ATGL expression and AMPK<sup>(14)</sup>.

## Conclusion

From above results, one can conclude that oral supplementation of resveratrol can result in improvement of anthropometric parameters in obese individuals. Future clinical studies needed to determine the effect of resveratrol on metabolic syndrome.

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