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Circulating Concentrations of Leptin Hormone, Soluble Leptin Receptor and Free Leptin Index in Obese Egyptian Women Before and after Diet Therapy

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It has been proposed that obesity is associated with resistance to the biological effects of leptin hormone. The aim of this study was to demonstrate the effect of obesity on both serum leptin and its soluble receptor and to evaluate the effect of consumption of a special food formula combined with a restricted diet for obesity management. Thirty-two obese women volunteered to test a natural food formula in combination with a balanced hypo caloric-diet (both supply 900-1000 Kcal day^{-1}) shared in a short term study, which lasted for four weeks. The formula was composed of whole sweet potato and carrot which were reduced to a flour form in 2:1 ratio and consumed as a pudding (20 g flour +100 mL boiled skimmed milk) for daily breakfast. Sweet potatoes and carrots are considered as a good source of dietary fibers, complex carbohydrates, antioxidants and phytochemicals. Subjects were divided into twenty-two obese women (group 1) with mean age (41.8±2.91 years) and body mass index (34.87±1.21), who followed the diet plus the pudding mixture; while ten obese women as a control (group 2) had a mean age of (43.4±2.28) and a body mass index of (36.57±1.31); who only followed the same diet. Relevant anthropometric measurements together with some biochemical parameters were determined before, after two and four weeks from the start of the regimen. Results showed although both groups lost weight comparably, group 1 ($p<0.01$,-3.55%), group2 ($p<0.01$,-2.01%), yet there were differences between them regarding serum leptin where in group 1 it was significantly decreased ($p<0.01$, -29.77%), with a concurrent increase in the serum soluble leptin receptor ($p<0.05$, +15.99%); in contrast to decreased levels of both leptin (-3.33%) and soluble leptin receptor ($p<0.001$, -5.05%) in group 2. Triglycerides levels were decreased ($P<0.05$,-22.62%) in group 1 in contrast to an increase ($p<0.05$, +39.40%) in group 2. In conclusion, incorporating custom-tailored food supplement in a slimming diet aiming at a quality weight loss that provides a healthier stable and durable metabolic environment should be considered.

Key words: Obesity, leptin, cytokine receptor family, soluble leptin receptor, adipose tissue, C-reactive protein

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INTRODUCTION

The worldwide prevalence of obesity is increasing at an alarming rate, with major adverse consequences for human health (Flier, 2004). Obesity is a public health challenge because it is associated with many complications, including type 2 diabetes, hypertension, coronary heart disease and increased mortality rate. Individuals diagnosed as clinically obese (Body Mass Index (BMI) >30 kg m^{-2}) suffer a mortality rate about three times as high as persons with BMI of under 24.9 kg m^{-2} (Calle *et al*., 1999). In recent years, several genes have been cloned that function in the control of body weight. Of these, the adipose tissue derived hormone leptin has emerged as a central component (Friedman, 2002). Leptin the protein product of the obese (ob) gene is produced primarily by the adipose tissue and is secreted into the circulation. It acts mainly on the hypothalamus and also on the other tissues through binding to specific leptin receptors which belong to the cytokine receptor family (Zhang *et al*., 1994; Tartaglia *et al*., 1995). Multiple isoforms of the leptin receptor family are generated through alternative splicing of the leptin receptor gene, including a long isoform expressed primarily in the hypothalamus; and several short isoforms with much wider tissue distribution (Tartaglia, 1997). A soluble form of leptin receptor, soluble leptin receptor (sOB-R), consisting of only extra-cellular region (Lee *et al*., 1996); binds leptin with an affinity similar to that of the membrane bound receptors (Lui *et al*., 1997). It represents the main leptin binding activity in the serum. This protein circulates in two different N-glycosylated isoforms, as dimer or in oligomerized state (Lammert *et al*., 2001). Experimental data are evident in humans showing that sOB-R is produced similarly by metalloprotease-mediated cleavage (Chua *et al*., 1997), whereas no mRNA for a splice form encoding the sOB-R has been detected (Hileman *et al*., 2002). It has been reported that the biological action of leptin is controlled by its soluble receptor, depending on certain metabolic and developmental conditions, at a molar excess of the sOB-R suppressive effects on leptin action may be important for energy uptake, states of the energy excess demonstrate an abundance of leptin over sOB-R in the circulation, which does not appear to be crucial for leptin action. Therefore, new tools affecting the energy balance of the organism via modulation of leptin action may be established (Zastrow *et al*., 2003). The ratio of serum leptin to sOB-R provides a measure of Free Leptin Index (FLI) which may be a more accurate determinant of leptin function, level of leptin and FLI conversely are primarily predicted by body composition (Misva *et al*., 2004). The reduction in the serum OB-R concentration in overweight and obese persons may reflect down regulation of hypothalamic leptin receptor production as a result of an increase in the circulating leptin and might be an important factor in leptin resistance (Hiroyuki *et al*., 2002). In the other study, it has been proposed that high fat diet impairs the sensitivity and physiological response to the satiety inducing adiposity hormone, leptin, thereby contributing to a syndrome similar to what can be observed in leptin deficient rodent or human (Ahima, 2006; Fazooqi and O' Rahilly, 2006). Because failure of leptin treatment for diet induced obesity has also been attributed to leptin resistance numerous efforts are still ongoing to better understand and ultimately prevent or cure leptin resistance (Ahima, 2006). Existing models have proposed a number of different mechanisms to explain the high-fat-induced development of leptin resistance, which is thought to be a pleiotropic phenomenon although it has mainly been examined with regard to leptin's action in the central nervous system (Munzeberg and Myers, 2005). The two most popular models explaining diet-induced-leptin resistance include, decreased transport of leptin across the blood brain barrier (Banks, 2006) and impaired intracellular leptin receptor signaling possibly a result of constant exposure to increased circulating amount of either dietary lipids or leptin itself (Munzeberg and Myers, 2005). Furthermore, it has been reported that triglycerides mediate leptin resistance; in the sense that triglycerides might act as an anti-anorectic agent during starvation. Decreasing triglycerides may potentiate the anorectic effect of leptin by enhancing leptin transport across the blood brain barrier (Banks *et al*., 2004). Other studies proposed that cereal-based diet could be such an environmental factor. Through previous studies in archaeology and molecular evolution it had been concluded that humans and human leptin system are not specially adapted to a cereal based diet and that leptin resistance associated with disease of affluence could be a sign of insufficient adaptation to such a diet. It has been proposed that lectins as a cereal constituent with sufficient properties to cause leptin resistance either through effects on metabolism central to the proper function of leptin system, and/or human leptin receptors, thereby affecting the function (Jonsson *et al*., 2005). Further studies reported that chronically elevated high sensitive C-reactive protein (hsCRP), a state of chronic inflammation, has been found to be positively correlated with adiposity as well as with leptin level. In addition leptin resistance may be partially attributed to interactions between leptin and a plasma circulating factor. It has been reported that CRP not only binds to plasma leptin but also impairs leptin signaling and attends its physiological

effect *in vivo*. For obese individuals reduction of CRP is an important target (Chen *et al*., 2006). The aim of this study was to demonstrate the effect of obesity on both serum leptin and its soluble receptor among obese Egyptian women and to evaluate the effect of consumption of a special natural food formula that was designed to be used in combination with hypo-caloric regimen for obesity management.

MATERIALS AND METHODS

Subjects: Thirty two obese women shared in this study which lasted for four weeks. They were recruited from the National Research centre, Cairo Egypt as volunteers. They were divided into two groups. Group 1 twenty two obese women with mean age (41.8±2.91 years) and BMI (34.87±1.21). They followed a low caloric balanced diet (900-1000 kcal) plus the pudding mixture. Group 2 ten obese women as a control had mean age of (43.4±2.28) and BMI of (36.57±1.31); they followed the same hypo-caloric balanced regimen only. All individuals were subjected to thorough clinical examination. Relevant anthropometric measurements were taken including weight, height, waist and hip circumference using standard methods (Jelliffe, 1966). BMI (weight in kg/height^2 in m) and Waist to Hip Ratio (WHR) were calculated. Blood pressure was measured, using mercury sphygmomanometer. Three readings were recorded, the mean of the second and third (systolic) and fifth (diastolic) Korotkoff sounds were used.

Blood sampling and biochemical analysis: Fasting blood samples were obtained from the women before regimen, after 2 weeks and lastly at the end of 4 weeks. The samples were taken in the morning after 12 h fasting. Hemoglobin concentration was measured in fresh samples by using cynomethaemoglobin method (Van Kampen and Zijlstra, 1961). The rest of the blood samples were allowed to clot at room temperature, centrifuged and sera were separated. Blood glucose was determined in fresh sera by using oxide peroxidase method (Barham and Trinder, 1972). The remaining sera were stored at -20°C until used for further analysis. Serum total cholesterol, HDL-C and triglycerides were done using: cholesterol proceed No 1010, Stanbio, HDL-C proceed No 0599 and stanbio Liquicolor triglycerides proceed No 2100, respectively. Friedewald formula was used to calculate LDL-C; LDL-C= (Total cholesterol)-(HDL-C)-(Triglyceride/5). hsCRP was measured by High sensitive C-reaction protein ELISA kit. Biocheck, Inc, 323 vintage parks Drive, Foster City, CA 94404. Serum leptin receptors were measured by Human Leptin Receptors ELISA kit. Cat No.: RD 194002100 R. Bio Vender-Laboratorni medicina a.s. Tumova 2265/60 CZECH REPUBLIC. Serum Leptin was determined by Leptin (Sandwich) ELISA. DRG Instruments GMGH. Germany.

Materials: A formula that was designed in this study was prepared from whole sweet potatoes and carrot flour, added to each other in certain amount (2:1). The two vegetables were dried at low temperature (40°C) with circulating air and then grind in powder form. Ginger and cinnamon were used as a flavor. A package containing 300 g of the mixture was given to every subject to be used over 2 weeks (20 g day^{-1}). The flour was used to prepare a pudding by adding 100 mL boiled skimmed milk and then consumed instead of breakfast bread.

Chemical food analysis: Chemical food analysis of the mixture was undertaken for: Macronutrients; including protein, fat, carbohydrate and fiber; using Association of Official Analysis Chemists (AOAC, 1990). Dietary fiber determination was done using AOAC (1997). Micronutrients including: minerals; calcium, iron, sodium, potassium and zinc using Atomic Absorption Apparatus Varian Spectr. AA,220 (Hussein and Burggeman, 1997) and beta carotene using high performance liquid chromatography (HPLC) 1100 series (Agilent technology) analysis (Leonardi *et al*., 2000).

Statistical analysis: All values are expressed as Mean±SEM by using SPSS (Chicago, IL, USA) software for windows (SPSS Inc., Chicago, IL, version 13.0, 2004).

RESULTS

Table 1 showed the chemical analysis of the pudding mixture (100 g dried weight) as regard their macro-and micro-nutrient contents. The data obtained showed its high contents of the dietary fiber (21.5 g), potassium (1498.5 mg), Zinc (5.16 mg) and B-Carotene (145 mg),

Table 1: Chemical analysis of dried weight of some macro-and micronutrient of the formula (100 g)

Nutrient	Amount
Moisture	8.60
Protein (g)	2.40
Fat (g)	1.41
CHO (g)	61.99
Ash (g)	5.30
Fiber (g)	0.29
Dietary fiber (g)	21.46
Calcium (mg)	173.50
Iron (mg)	6.97
Sodium (mg)	406.30
Potassium (mg)	1498.50
Zinc (mg)	5.16
Beta carotene (mg)	145.00

besides its low sodium content (406.3 mg). Table 2 showed Mean±SEM of the recorded age, anthropometric parameters and blood pressure, before, during and at the end of the study. Body weight showed significant reduction among both groups. Waist, hip and WHR showed significant decrease which was higher among group 1, as it decreased by 4.12% at the end of the study. Systolic blood pressure showed significant decrease at both the mid and last visit, while diastolic blood pressure showed significant reduction at the end of the study among group 1. Table 3 showed the Mean±SEM of the investigated biochemical parameters. Significant increase was reported in hemoglobin concentration at $p<0.05$ among group 1 at the mid and the end of the study. Numerical decrease was found in the glucose level among group 1 compared to numerical increase between obese women of group 2. TC and LDL-C concentrations were significantly decreased among group 2 but numerically among group 1. HDL- C was increased in both groups, the higher significant increase at $p<0.01$ and <0.05 was reported at the end of the study between obese women of group 1. TG was beneficially significantly decreased by-20.22 and 22.62% between group 1. Table 4 showed the Mean±SEM of the investigated biochemical parameters. hsCRP concentration showed variable results, numerically decreased at the end of the 2nd week and increased at the end of the 4th week between both groups. Pudding dieters showed a reduction in the serum leptin concentration starting by the end of the 2nd week which persisted and reached a considerable decrease ($p<0.001$) at the end of the study. Also the calculated FLI showed high percent decrease (-69.64% and -73.82%) among the

Table 2: Mean±SEM of the age, anthropometric measurements and blood pressure of obese woman, before, during and after regimen

	Pudding (group 1) No.: 22					Control (group 2) No.: 10				
				Change (%)					Change (%)	
	1st	2nd	3rd	1st	2nd	1st	2nd	3rd	1st	2nd
Parameters	(Mean±SE)					(Mean±SE)				
Age (years)	41.18±2.19					43.40±2.28				
Height (cm)	157.18±0.78					155.20±1.22				
Weight (kg)	86.23±3.13	84.27±3.15[3]	83.15±3.27[3,6,9]	-2.27	-3.55	87.90±3.66	86.80±3.41[1]	86.13±4.29[5,9]	-1.25	-2.01
BMI (kg m^{-2})	34.87±1.21	34.08±1.22[3]	33.67±1.26[6,9]	-2.27	-3.44	36.57±1.31	36.01±1.25[2]	35.82±1.57[5,9]	-1.53	-2.05
Abd1 Cir. (cm)	93.50±2.41	90.23±2.50[3]	89.65±2.69[6,9]	-3.50	-4.12	94.50±2.76	93.10±2.76[3]	92.50±3.48[6,9]	-1.48	-2.12
Hip Cir. (cm)	119.32±2.33	117.18±2.24[3]	116.85±2.33[6,9]	-1.79	-2.07	118.60±2.28	117.50±2.27[3]	116.88±2.69[6,9]	-0.93	-1.45
WHR (cm)	0.78±0.009	0.77±0.01[1]	0.76±0.01[5,9]	-1.28	-2.56	0.79±0.01	0.79±0.01[2]	0.78±0.01[5,7]	-	-1.27
SBP (mm Hg^{-1})	132.50±4.05	129.50±3.13[1]	128.89±3.74[4]	-0.77	-1.23	126.00±4.87	122.00±5.01	123.75±4.89	-3.17	-1.79
DBP (mm Hg^{-1})	83.50±1.85	83.50±1.45	81.11±1.24[5,7]	-	-2.86	81.00±2.21	80.00±2.11	80.00±2.67	-1.23	-1.23

[1,2,3]Significantly different from baseline vs. second: [1]$p<0.05$, [2]$p<0.01$, [3]$p<0.001$, [4,5,6]Significantly different from baseline vs. third: [4]$p<0.05$, [5]$p<0.01$, [6]$p<0.001$, [7,8,9]Significantly different from second vs. third: [7]$p<0.05$, [8]$p<0.01$, [9]$p<0.001$

Table 3: Mean±SEM of biochemical parameters among obese women, before, during and, after regimen

	Pudding (group 1) No.: 22					Control (group 2) No.: 10				
				Change (%)					Change (%)	
	1st	2nd	3rd	1st	2nd	1st	2nd	3rd	1st	2nd
Parameters	(Mean±SE)					(Mean±SE)				
Haemoglobin (g dL^{-1})	12.06±0.37	13.20±0.342	12.85±0.30[4]	+9.45	+6.55	13.88±0.17	14.09±0.26	14.35±0.264	+1.51	+3.39
Fasting blood sugar (mg dL^{-1})	87.67±2.91	83.09±2.47	82.89±4.07	-5.22	-5.45	82.70±4.98	86.89±2.65	85.98±4.47	+5.07	+3.97
T. Cholesterol (mg dL^{-1})	230.53±9.67	226.13±5.64	229.35±11.86	-1.91	-0.51	273.39±13.73	249.85±6.53	241.20±15.47	-8.61	-11.77
HDL.C (mg dL^{-1})	52.66±2.13	55.29±2.74	58.39±2.29[5,7]	+4.99	+10.88	48.42±2.11	52.38±2.25[1]	55.77±4.27	+8.18	+15.18
LDL.C (mg dL^{-1})	156.89±7.67	163.15±8.35	154.47±10.5	+3.99	-1.54	203.81±12.76	175.14±6.01[1]	150.78±13.25[4]	-14.07	-26.02
Triglycerides (mg dL^{-1})	104.78±11.61	83.59±9.452	81.08±5.56[4]	-20.22	-22.62	106.56±13.25	120.00±21.29	148.54±25.93[4,8]	+12.61	+39.40
Risk factor	4.44±0.19	4.40±0.36	4.03±0.26[4]	-0.90	-9.23	5.77±0.39	4.88±0.29[2]	4.46±0.39[5]	-15.42	-22.70

[1,2,3]Significantly different from baseline vs. second: [1]$p<0.05$, [2]$p<0.01$, [3]$p<0.001$, [4,5,6]Significantly different from baseline vs. third: [4]$p<0.05$, [5]$p<0.01$, [6]$p<0.001$, [7,8,9]Significantly different from second vs. third: [7]$p<0.05$, [8]$p<0.01$, [9]$p<0.001$

Table 4: Mean±SEM of biochemical parameters among obese women, before, during and, after regimen

	Pudding (group 1) No.:22					Control (group 2) No.:10				
				Change (%)					Change (%)	
	1st visit	2nd visit	3rd visit	1st	2nd	1st visit	2nd visit	3rd visit	1st	2nd
Parameters	(Mean±SE)					(Mean±SE)				
C-reactive protein (mg dL^{-1})	6.44±0.45	5.59±0.54	7.04±0.45[8]	-13.20	+9.32	5.48±0.38	4.77±0.45	5.50±0.86	-18.43	+0.36
Leptin (ng mL^{-1})	26.07±3.64	23.21±3.42	18.31±2.69[6,8]	-10.97	-29.77	24.03±3.47	19.36±3.16	23.23±4.53	-19.43	-3.33
Leptin receptor (ng mL^{-1})	21.64±2.78	29.32±2.91[2]	25.10±2.36[4,8]	+35.49	+15.99	21.20±4.72	20.20±3.51	20.13±3.39[6]	-4.72	-5.05
Free leptin index (FLI)	3.59±1.46	1.09±0.21	0.94±0.17[8]	-69.64	-73.82	1.80±0.43	1.38±0.37[1]	1.59±0.38[2]	-23.30	-11.67

[1,2,3]Significantly different from baseline vs. second visit: [1]$p<0.05$, [2]$p<0.01$, [3]$p<0.001$, [4,5,6]Significantly different from baseline vs. third visit: [4]$p<0.05$, [5]$p<0.01$, [6]$p<0.001$, [7,8,9]Significantly different from second vs. third visit: [7]$p<0.05$, [8]$p<0.01$, [9]$p<0.001$

Table 5: Correlation coefficient between BMI and biochemical parameters among both groups at different periods of intervention

	Pudding (group 1) No.: 22						Control (group 2) No.: 10					
	1st		2nd		3rd		1st		2nd		3rd	
Parameters	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value
BMI												
Sugar	-0.016	NS	0.047	NS	0.669**	<0.01	-0.580	NS	0.198	NS	-0.736*	p<0.05
Cholesterol	0.524*	<0.05	0.335	NS	0.412	NS	0.281	NS	0.804**	<0.01	-0.152	NS
HDL-c	0.495*	<0.05	0.118	NS	-0.179	NS	-0.675*	<0.05	-0.832**	<0.01	0.005	NS
LDL-c	0.466*	<0.05	0.516*	<0.05	0.455*	<0.05	0.324	NS	0.796**	<0.01	-0.421	NS
Triglycerides	0.524*	<0.05	0.352	NS	0.509*	<0.05	0.509	NS	0.476	NS	0.448	NS
hsC.R.P	0.479*	<0.05	-0.050	NS	-0.441	NS	-0.476	NS	0.632*	<0.05	0.235	NS
Leptin	0.608**	<0.01	0.775**	<0.01	0.849**	<0.01	0.805**	<0.01	0.819**	<0.01	0.946**	<0.01
Leptin receptor	-0.419	NS	-0.473*	<0.05	-0.534*	<0.05	-0.532	NS	-0.281	NS	-0.898**	<0.01
FLI	0.761**	<0.01	0.902**	<0.01	0.916**	<0.01	0.865**	<0.01	0.628*	<0.05	0.896**	<0.01

NS: Non significant, *Correlation is significant at the 0.05 1evel (2-tailed), ** Correlation is significant at the 0.01 level (2-tailed)

same group, at the two studied periods. The control group showed a lesser and insignificant decrease in the leptin level but significant decrease in FLI (-23.3 and -11.67%). sOB-R concentration significantly increased by 3.49 and 15.99% between obese women of group 1 compared to the decrease reported in its concentration among the control group. Table 5 showed the correlation coefficient between BMI and the studied biochemical parameters. Among obese women of group 1, BMI showed positive significant correlation after the first 2 weeks with LDL-C, leptin and FLI; and negative significant correlation with sOB-R. The same results were observed at the end of the study in addition to significant positive correlation between BMI and both glucose and triglycerides concentration. At the mid visit obese women of group 2 showed positive significant correlation with TC, LDL-C, hsCRP, leptin and FLI. Significant negative correlations were reported with HDL-C. At the end of the study the control group showed significant negative correlation with both glucose and sOB-R.

DISCUSSION

The results of this study showed that the obese women exhibited a mild elevation in the concentration of both TC and LDL-C, while the fasting blood glucose level was within the normal range. Obese patients showed high level of leptin hormone with a mild decrease in the sOB-R. High sensitive CRP concentration was high indicating an inflammatory condition. The role of adipose tissue as inductive of a state of chronic low-grade inflammation, where markers of inflammation such as pro-inflammatory cytokines and acute phase proteins are increased in the circulation is confirmed (Trayhurn and Wood, 2004). It is now thought that inflammatory state may be causal in the development of insulin resistance and another disorders associated with obesity such as the metabolic syndrome and hyper-lipidemia (Yudkin, 2003). In this study we introduced a newly designed formula to be used in the form of pudding made from sweet potato flour and carrot, each added in a certain amount (2:1), to replace breakfast bread, besides using a hypo-caloric diet. The purpose of this trial was to reduce weight and in the same time limit the inflammatory status among the obese women, in addition to improving both leptin and sOB-R concentration. Carrot and sweet potato are good sources of complex carbohydrate, dietary fiber, very low in saturated fat and cholesterol, low in sodium high in potassium, good source of vitamin B, C and beta-carotene (Ensminger *et al*., 1983). Beta-carotene as a phytochemical has shown antioxidant activities, however its molecular mechanism has not been clearly defined. In addition, it has been suggested that beta-carotene possesses anti-inflammatory activity probably due to its antioxidant properties (Bai *et al*., 2005). It is suggested that 33 kDa TI, one of the sweet potato root storage proteins, may play a role as an antioxidant in root and may be beneficial to health when it is consumed (Ajani *et al*., 2004). Further, more it was found that fiber intake is independently associated with CRP concentration and support the recommendation of diet with high fiber content (Ajani *et al*., 2004). The data obtained after the intervention program showed favorable effects on most of the risk parameters studied. Significant decreases in body weight and BMI were reported, in addition to the decrease in the waist circumference that was more prominent among group 1, which is a good marker of the reduction of potential exposure to cardiovascular disease (Haffner *et al*., 2006). The effect of the intervention program on the blood lipid profiles was quite apparent. A satisfactory decrease in the mean concentration of TG and elevation in the mean HDL-C concentration were observed. The calculated risk factor (TC/HDL-C) also decreased between both groups. On the other hand, triglycerides level showed significant decrease among obese women of group 1, while its concentration

significantly increased between obese women of group 2. The high fiber formula and its content of complex carbohydrate that was consumed by the first group could improve the triglyceride level in such cases (Banks *et al*., 2004). The data obtained from this study revealed high Leptin concentration and low sOB-R among the obese women. The sOB-R is the main leptin binding protein and the relation between the serum leptin and sOB-R provides a measure of the Free Leptin Index (FLI), which may be a more accurate determinant of leptin function (Misva *et al*., 2004). sOB-R may act as a negative regulator of leptin activity and it may maintain a pool of available bioactive leptin by binding and delay its clearance from circulation (Zastrow *et al*., 2003). It has been suggested that in obese individual the majority of leptin circulates in the free form presumably bioactive protein and thus obese subjects are resistance to free leptin (Sinha *et al*., 1996). The reduction in sOB-R concentrations in overweight and obese persons may reflect down regulation of hypothalamic leptin receptor production as a result of an increase in the circulating leptin and might be an important factor in leptin resistance (Hiroyuki *et al*., 2002). After intervention leptin concentration and FLI significantly decreased, while sOB-R significantly increased among obese women of group 1, while numerical decrease was detected in the leptin level and FLI as well as sOB-R between obese women of group 2. It has been reported that the modest decrease in the energy intake sustained over several weeks may play an important role in altering levels of plasma leptin and sOB-R (Wolfe *et al*., 2004). Furthermore, the level of leptin and FLI are primarily predicted by body composition. Markus *et al*. (2002) reported that women experienced significant reduction in the body mass index and fat mass after surgery showed a significant decrease in the plasma leptin concentration and concurrent increase in sOB-R level, resulting in an increase of the receptor bound fraction of leptin from 7 to 33% (Wolfe *et al*., 2004). This is in agreement with the data in this study which showed a high positive significant correlation between BMI and both leptin and FLI, while a significant negative correlation between it and sOB-R was reported. However the difference detected between the two obese groups, in this study concerning these parameters; first it may be attributed to the great significant decrease in the triglycerides level that was confirmed in obese women of group 1. Serum triglycerides are elevated in both starvation and obesity, it was postulated that triglycerides inhibit leptin transport across BBB. Manipulation of triglycerides level with diet or fasting in normal or obese mice had an inverse effect on leptin transport and that reduction of triglycerides by pharmacological intervention reversed the impairment in the leptin transport (Banks *et al*., 2004). Taken together, these findings and the data of this study showed that triglycerides could inhibit the transport of leptin across BBB and so could be a major cause of leptin resistance. Second, according to the presumption that chronic inflammatory state accompanies adiposity (Trayhum and Wood, 2004), data obtained in this study showed some variations in the level of the hsCRP. After the first two weeks of intervention and weight reduction, there was a slight decrease in the mean level, but after the end of the four weeks, slight increase in the mean level was detected. However, intragroup variation was found among the obese patients, as 50 and 40 % of the obese women of group 1 showed a decrease in the level of the hsCRP at the mid and last visit, while 60 and 25% of the obese women of group 2 showed similar results. Trayhum and Wood (2004), focus on the role of adipose tissue as a source of the protein characteristic by a state of chronic low grade inflammation. In addition adipose tissue seems to have an indirect role; hepatic production of CRP may be stimulated by the increased release of the interleukin-6 from adipocytes. A relation between CRP and leptin resistance was postulated, human CRP inhibit human leptin signaling in leptin triggered Janus family tyrosine kinase (JAK), signal transducers and activators (STAT) and PI3K pathway in rat primary hypothalamic neuron (Well *et al*., 2005). So, in this context the highly antioxidant properties of the supplement used by obese women of group 1 may play a role in limitation of the inflammatory status of the white adipose tissues in considerable number (40%) of them which lead to decrease concentration of hsCRP and subsequently leptin level. Plant pigments such as carotenoids tend to dampen inflammation (Bai *et al*., 2005).

In conclusion these optimistic results obtained in this study could be due to decrease energy intake and to the improvement in body weight. In the same time it could be attributed to the supplement used with the hypo-caloric diet. Sweet potatoes and carrots are considered as a good source of dietary fibers, complex carbohydrates, antioxidants and phytochemicals. The experimental protocol and diet therapy generally reduced triglycerides and inflammation and improved both leptin hormone, FLI and the sOB-R concentration.

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