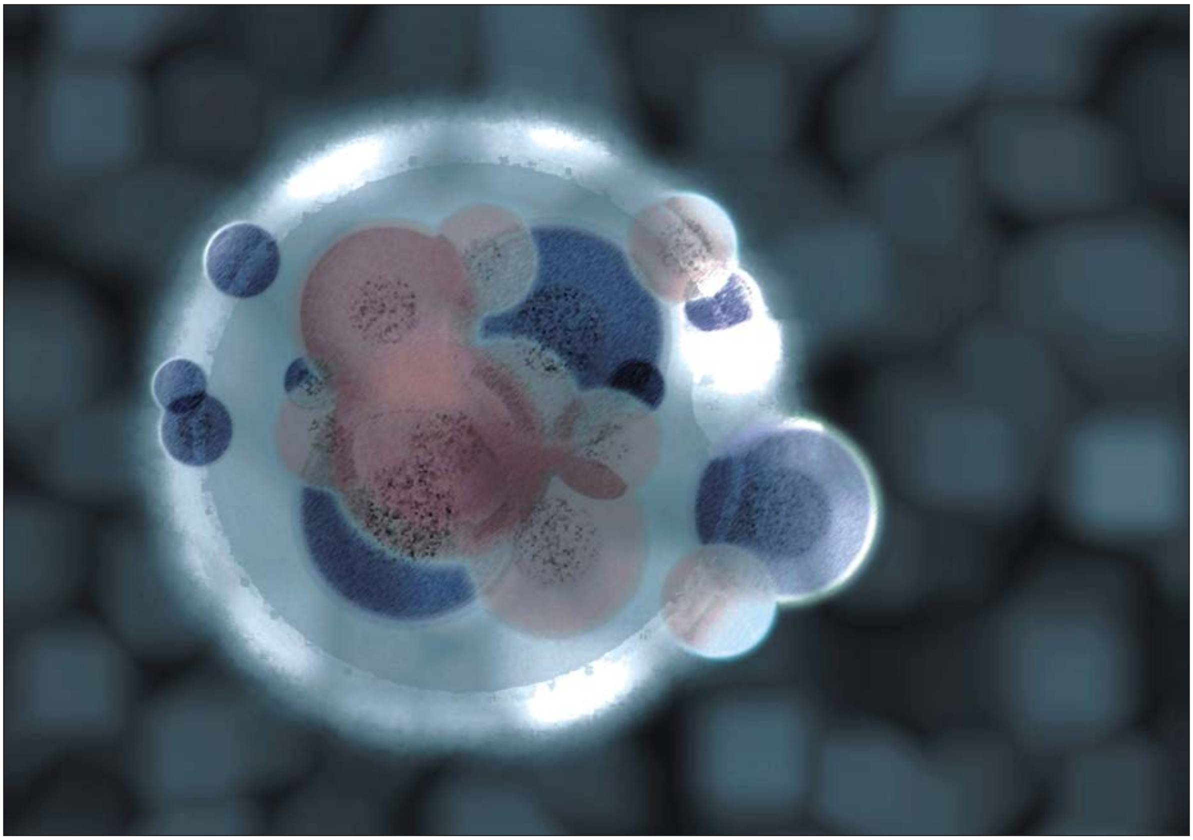

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Research Article
Relation Between Obesity, Cognition and Serum Amyloid β Protein Level and Potential Role of *Foeniculum vulgare* in Reducing Weight and Improving Cognitive Functions

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Abstract
Background and Objective: Epidemiological studies show that obese patient have an increased risk for cognitive functions impairment. Reports stated that serum amyloid beta (Aβ) peptide levels may reach its peak during the early stage of Alzheimer's disease (AD). The objective of study was to recognize if the plasma Aβ can be applied as biomarker for cognitive function impairment and to demonstrate the effect of using supplements having bioactive components (whole wheat, fennel and chia seeds) with a balanced hypocaloric regimen, on the cognitive functions of middle aged obese women, in addition to their effect in reducing body weight. **Materials and Methods:** One hundred and forty middle age obese women suffering from different degrees of obesity volunteered in this study which lasted for 8 weeks. All patients were following a balanced low caloric diet (900-1000 calorie/day). The participants were divided into 3 groups: Group (A) consumed fennel supplement, group (B) consumed chia seeds supplement and group (C) consumed baladi bread. Evaluations were made at baseline and 8 weeks later. This included clinical examination, anthropometric measurements, determination of internal metabolic profile, serum Aβ protein and cognitive evaluation. All values were expressed as mean value±SE. Paired-sample t-tests were used to compare the data in the same group before and after dietary therapy. The obtained results of different supplement formulae were evaluated statistically using one-way-ANOVA. **Results:** After intervention, improving in cognitive functions decrease in serum Aβ protein and improving of the metabolic profile and body weight, especially with fennel supplement were recorded. **Conclusion:** It is concluded that dietary therapy especially using fennel seed proved to be effective in reducing body weight, improving metabolic profile and cognitive functions. Serum Aβ protein level may be used as a marker for cognitive functions impairment in the obese middle age female.

Key words: Amyloid beta protein, cognitive function, dietary supplement, fennel, obesity

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Actually, there are over 30 million dementia patients all over the world[1]. The existing theoretical models hypothesized that the changes in plasma amyloid beta (Aβ) levels, hippocampal atrophy, cognitive loss and C-reactive protein were previously observed up to 10 years before diagnosis. Acceleration in cognitive decline seems to follow a significant increase in amyloid accumulation and depressive symptomatology remains at a constantly higher level. Overall, biological and clinical markers do not follow the same route, the distance from dementia controls the changes of the clinical picture[2]. He *et al.*[3] reported that serum Aβ peptide levels may reach its peak during the early stage of Alzheimer's disease (AD). Monitoring serum Aβ peptide levels in the potential AD population may affords early diagnosis of AD before the appearance of clinical symptoms.

A lot of studies have proved that there is a strong association between higher concentration of plasma Aβ and aging[4,5]. However, there are conflicting results, some studies finding an association[6,7] and others are not[8,9]. Two studies have evaluated the hereditability of Aβ plasma levels. A study by Ertekin-Taner *et al.*[10] found a higher (54% for a hereditability β_{1-40} and 73% for $A\beta_{1-42}$) than the one by Ibrahim-Verbaas *et al.*[11] reported (23% for $A\beta_{1-40}$ and 30% for $A\beta_{1-42}$).

In some pathological condition as type 2 diabetes, the pro-inflammatory signaling and prolonged metabolic stress lead to attenuation of the insulin signaling and decreased cellular responsiveness to insulin, which result in the development of a state of insulin resistance and impairs the ability of the cells to maintain energy homeostasis[12]. Similar abnormalities present in AD brain, including neuroinflammation and metabolic stress[13-17]. In this context, Li *et al.*[18] suggested that aging is a factor related to the risk of AD where high concentration of $A\beta_{40}$ and low insulin concentration were observed.

Toledo *et al.*[19] stated that tau and amyloid beta (Aβ), in cerebrospinal fluid are a reliable diagnostic marker for AD and can denote the neuropathologic condition. However, the measurement of Aβ in plasma would be the least invasive and most cost-effective biomarker assay. Plasma Aβ can be applied as trait, risk or state biomarkers for AD[5]. In the same time, one study has reported the presence of a stronger correlation between plasma Aβ and positron emission tomography (PET) or Pittsburgh Compound-B-C11 (PiB) as radiotracers illustrates fibrillar brain amyloid deposits which is a reliable method to measure brain amyloid plaque accumulation[20,21].

Cereal-based foods are key components of the diet. Slavin *et al.*[22] reported that whole grain foods are good sources of nutrients as B vitamins, vitamin E, selenium, zinc, copper, magnesium and dietary fiber. Phytochemicals, such as phenolic compounds are valuable components of whole grains that together with vitamins and minerals have important roles in prevention of many diseases.

There were evidence supports a possible involvement of lipid levels in the development of dementia and AD, suggesting dyslipidemia as one of the modifiable risk factors to be targeted by therapeutic interventions which are already widely available[23].

Fennel *(Foeniculum vulgare)* is one of the most important medicinal plants grown within the Mediterranean region, in Europe and in Egypt. This plant belongs to *Umbelliferae* (*Apiaceae*) family which is known and used by humans since antiquity. The essential oil of fennel have many medical benefits as it can be used as antispasmodic, diuretic, anti-inflammatory, analgesic and antioxidant[24,25]. Natural antioxidants have several functions as they can protect the human body from free radicals and may protect from many chronic diseases, also the retard of lipid oxidative rancidity in foods[26].

Chia seeds (*Salvia hispanica*), more commonly known as chia, is a traditional food in Central and Southern America. Chia seeds contain various active ingredients including essential fatty acids especially α-linolenic acid (ALA) and phenolic compounds[27]. At the present time chia is widely used to achieve several health benefits specifically in maintaining healthy lipid level.

The aim of this study was to demonstrate the effect of using two supplements, one made mainly from whole wheat flour mixed with 10% fennel powder and the other composed of whole wheat flour mixed with 10% chia seeds in conjunction with a balanced hypocaloric regimen, on the cognitive functions of middle age obese women, in addition to their effect in reducing body weight. Cognitive functions measured by both biochemical parameter (Aβ protein) and by oral test.

MATERIALS AND METHODS

The study was conducted through a project funded by National Research Centre (NRC) Egypt, 2013-2016, entitled" Detecting modifiable risk factors for cognitive function impairment and dementia among obese middle age Egyptians and studying dietary long term measures for prevention".

Materials: Whole meal wheat grains (Giza 168) was purchased from Wheat Research Department, Field Research Institute, Agric. Res. Centre, Giza, Egypt. Fennel seeds were obtained from local shop, Dokki, Egypt and milled to form powder. Chia seeds, skimmed milk, flax seed oil and baking powder were purchased from the local market, Dokki, Egypt.

Analytical methods: Basic and modified formulae were prepared by mixing the whole meal wheat flour (100% extraction) with fennel seeds powder (*Foeniculum vulgare*) at the levels of 5% (formula 1) and 10% (formula 2) with other ingredients. The other formulae were prepared of whole wheat flour with 5% (formula 3) and 10% (formula 4) chia seeds (*Salvia hispanica*) mixed with other ingredients according to Table 1. About 14.7 mL of dextrose solution (5.93%) and the suitable amount of water were added according to AOAC[28], to be formed as cookies each weighing 20 g. These formula was baked in a special oven at 200°C for about 15 min. Weight, volume, specific volume, diameter, thickness and spread ratio of the bread were recorded. According to Hussein and Ali[29], the panel test was carried out, the cookies made from 10% fennel powder (formula 2) and 10% chia seeds (formula 4) were the choice.

Chemical composition of the different formula: Moisture, protein, fat, crude fiber and ash of the four formulae were determined according to AOAC[28]. Carbohydrates were calculated by differences. The mineral and fatty acids content in raw fennel, chia and the two types of cookies that consumed by the participants (10% fennel and 10% chia) were determined using standard methods[30,31].

Organoleptic characteristics: Organoleptic characteristics of all samples were evaluated according to Hoojjat and Zabik[32], where each formula was subjected to sensory analysis by 20 panelists. Each panelist was asked to assign scores 0-20 for color, odor, taste, texture, appearance and overall acceptability (0-100).

Subjects: One hundred and forty obese women suffering from different degrees of obesity participated as volunteers in this study which lasted for 8 weeks. The participants were informed about the purpose of the study and their permission in the form of written consent was obtained. The protocol was approved by the "Ethical Committee" of the "National Research Centre".

The participants were divided into 3 groups, group (A): 50 women with mean age of 49.82±1.31 years and mean body mass index (BMI) of 35.78±0.81 kg m^{-2}, group (B): 46 women with mean age of 51.60±1.02 years and mean BMI of 37.52±0.78 kg m^{-2} and group (C): The control group, 44 women with mean age of 48.21±1.58 years and mean BMI of 37.58±1.05 kg m^{-2}. Group (A) followed a low caloric balanced diet (1000-1200 K calories/day), accompanied by the supplement made from whole wheat flour mixed with 10% fennel powder that was made in the form of cookies, four services were consumed/day, two with breakfast (40 g) and two with dinner (40 g), instead of Baladi bread. Group (B) consumed another formula of the cookies made from the whole wheat flour mixed with 10% chia seeds with the same instructions. The control group (C) followed only the same low caloric balanced diet using baladi bread that gave the same amount of calories as the supplements. All women were subjected to thorough clinical examination.

The following investigations were performed at the start of the study (Basal visit) and after 8 weeks (Last visit):

Anthropometric parameters and blood pressure measurements: Relevant anthropometric measurements were reported according to Hiernaux and Tanner[33]. Body mass index (BMI) was calculated (weight in kg/height in m^2). Body fat (BF) as a percent from the body weight was measured using geratherm body fitness (B-5010), German. Blood pressure for each subject was measured 3 times and the mean was recorded. All measurements were taken by the same researcher to assure accuracy.

Blood sampling and biochemical analysis: Fasting blood samples (after 12 h fasting) were drawn from the patients. Hemoglobin concentration was measured by using cyanmethemoglobin method[34]. The rest of the blood samples were allowed to clot at the room temperature, centrifuged and sera were separated. Fasting blood glucose (FBG) was determined on fresh samples using glucose oxidase method[35], other biochemical parameters were performed on fasting sera that were stored at -70°C until used. The levels of serum total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were measured using, cholesterol proceed No 1010, StanbioLiquicolor[36], HDL-C

Table 1: Formula composition of the cookies (g/100 g dry weight)

Raw materials	Formula (1)	Formula (2)	Formula (3)	Formula (4)
Whole wheat flour	75	70	75	70
Fennel powder	5	10	-	-
Chia seeds	-	-	5	10
Skimmed milk	10	10	10	10
Flax seed oil	5	5	5	5
Baking powder	5	5	5	5

proceed No 0599 StanioLiquicolor[37] and triglycerides proceed No 2100[38], (Enzymatic method), respectively. Low density lipoprotein-cholesterol (LDL-C) was calculated according to Friedewald equation:

$$\text{LDL-C} = (\text{TC})\text{-}(\text{HDL-C})\text{-}(\text{TG}/5)^{39}$$

$$\text{Non-HDL-C} = (\text{TC})\text{-}(\text{HDL-C})$$

and

$$\text{Risk factor} = (\text{TC})/(\text{HDL-C})$$

were calculated.

Serum β amyloid protein was assessed using Human Amyloid beta A4 protein ELISA kit, catalog no. E0946h supplied by EIAab Science Co., Ltd, Wuhan, China[40].

Dietary recalls: Data on dietary intake were performed using the 24 h dietary intake recall. The total dietary intake was analyzed using the Nutrisurvey[41] computer program.

Cognitive and mental evaluation: After the first visit evaluation, the patients were classified into 3 groups. The following tests were done:

Mini mental state examination (MMSE) was performed for evaluation of mental and cognitive status. The MMSE was the most commonly used test for complaints of memory problems[42]. It was a sensitive, valid and reliable 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It was also used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time, thus making it an effective way to document an individual's response to treatment. Administration of the test takes between 5-10 min and examines functions including registration, attention and calculation, recall, language, commands andorientation[43].

Life style questionnaire: A questionnaire designed to evaluate life style through questioning: General subjective life stresses, mood, appetite, tea and coffee consumption, general activity and history of exercising were recorded and put on a 3 points scale.

Classification and scoring system: *MMSE (mini mental state examination): 22-25 =1, 26-28 = 2 and 29 = 3. *Mood: Bad = 1, regular =2 and good =3. *Tea and coffee consumption (number of cups/day): 0-1 = 1, 2-4 = 2 and 5-8 = 3. The following variables were classified as, stress, appetite, general activity, exercising: 1 = low, 2 = medium and 3 = high.

Statistical analysis: All values were expressed as Mean value±SE. Paired-sample t-tests were used to compare the data in the same group before and after dietary therapy. $p<0.05$ were considered statistically significant. The SPSS window software version 17.0 (SPSS Inc., Chicago, IL, USA, 2008) was used. The obtained results of different supplement formula were evaluated statistically using analysis of variance (one-way ANOVA) as reported by McClave and Benson[44].

RESULTS

The data regarding the average of moisture, protein, fat, crude fiber and ash of the different formula produced from mixture is summarized in Table 2. The protein, fat, fiber, moisture and ash in formula (2) were higher than formula (1), however, the total carbohydrate contents of formula (2) were lower than formula (1). The same trend was observed in formula (4) compared to formula (3).

The minerals' content and the relative areas (%) of fatty acids of the raw fennel powder and the raw chia powder, in addition to that of the two consumed supplements, the 10% fennel cookies (Formula 2, supplement 1) and the 10% chia cookies (Formula 4, supplement 2) was shown in Table 3.

Adding the whole wheat flour to fennel in supplement (1) enriched its mineral contents compared to supplement (2) and also increased its content of the eurcic, oleic, linoleic and linolenic fatty acids in various ranges. While in cases of chia seeds, only its content of oleic fatty acid increased.

Data presented in Table 4 shows the mean±SE and %RDA of the macro and micronutrient contents of the habitual diet of the whole studied sample before starting the

Table 2: Chemical composition of the cookies produced from the different formulae

Formula	Moisture (%)	Protein (%)	Ash (%)	Fat (%)	Fiber (%)	Total carbohydrates
1	20.77±0.19[c]	9.91±0.07[b]	2.79±0.05[c]	3.92±0.05[b]	2.32±0.15[c]	81.06±1.11[b]
2	22.98±0.11[b]	10.17±0.09[a]	3.08±0.03[b]	4.21±0.02[a]	2.91±0.15[b]	79.63±1.18[c]
3	21.82±0.22[a]	7.73±0.13[d]	2.38±0.07[d]	3.02±0.06[c]	2.57±0.15[c]	84.30±1.15[a]
4	23.08±0.13[d]	8.45±0.11[c]	3.22±0.04[a]	3.89±0.03[b]	5.01±0.15[a]	79.43±0.96[c]
LSD at 0.05	1.16	0.23	0.036	0.085	0.071	1.19

Results were expressed as Mean±SE, Means with different letters were statistically significant, 1: Cookies with 5% fennel powder, 2: Cookies with 10% fennel powder, 3: Cookies with 5% chia seeds and 4: Cookies with 10% chia seeds

Table 3: Minerals and fatty acids content of the tested samples

Parameters	Fennel blend raw	Chia blend raw	Cookies with 10% fennel (Formula 2, supplement 1)	Cookies with 10% chia (Formula 4, supplement 2)
Minerals (mg)				
Potassium	167.0	132.5	179.50	124.50
Sodium	130.5	137.0	168.00	184.50
Calcium	92.0	54.0	118.50	70.50
Magnesium	93.5	93.0	98.00	84.00
Iron	2.2	1.8	5.13	3.59
Zinc	1.1	0.9	1.42	0.98
Fatty acids (relative area %)				
Palmitic (C 16:0)	5.6	8.5	7.00	7.10
Stearic (C18:0)	-	-	6.00	10.10
Oleic (C18:1, n-9)	36.7	48.7	44.90	53.90
Linoleic C18:2, n-6)	3.8	5.5	5.90	5.60
Linolenic (C18:3, n-3)	5.5	4.4	9.50	1.10
Erucic (C22:1)	7.2	10.9	14.20	6.30

Table 4: Mean±SE and % of macro and micronutrients content of the different types of diet among the studied groups

Nutrient intake	Habitual diet Before regimen All subjects	Group (1) Diet with 10% fennel (Formula 2, supplement 1)	Group (2) Diet with 10% Chia (Formula 4, supplement 2)	Control group (3) Diet with Baladi Bread	RDA
Mean±SE and % RDA					
Energy (kcal)	1942.50±88.34	910.50±78.64	912.80±71.20	1059.30±94.54	2200
	88.29%	41.39%	41.49%	48.15%	
Protein (g)	76.10±28.14	37.90±29.24	37.91±26.21	52.10±30.24	50
	152.20%	75.80%	75.82%	104.20%	
Carbohydrate (g)	218.10±27.41	141.01±19.24	141.11±12.45	139.70±25.64	300
	72.70%	47.00%	47.03%	46.57%	
Dietary fiber (g)	24.80±5.14	32.71±9.87	34.51±6.75	28.40±9.34	25
	99.20%	130.84	138.04%	113.60%	
Fat (g)	82.50±21.71	20.4±8.67	20.6±10.12	30.90±12.19	65
	126.92%	31.38%	31.69%	47.54%	
Cholesterol (mg)	343.20±13.37	121.31±14.21	122.01±13.21	191.70±15.24	
Thiamin (mg)	0.69±0.30	0.87±0.17	0.86±0.12	0.85±0.52	0.9
	76.67%	96.67%	95.56%	94.45%	
Riboflavin (mg)	0.65±0.27	0.88±0.68	0.87±0.42	0.84±0.58	0.9
	72.22%	97.77%	96.67%	93.34%	
Niacin (mg)	7.48±2.34	10.77±3.83	10.75±2.87	9.71±3.90	11
	68.00%	97.91%	97.73%	88.27%	
Foliate (mg)	198.17±13.41	310.25±17.52	307.18±64	300.96±18.01	320
	61.93%	96.96%	95.99%	94.05%	
Vitamin B6 (mg)	0.61±0.38	0.99±0.22	0.97±0.42	0.93±0.33	1.1
	55.45%	90.00%	88.18	84.54%	
Vitamin B12 (mcg)	1.40±0.40	1.95±15.87	1.92±11.21	1.87±12.34	2
	70.00%	97.50%	96.00%	93.50%	
Vitamin A (µg)	761.10±33.97	786.76±30.57	787.31±25.67	784.90±31.89	800
	95.14%	98.35%	98.41%	98.11%	
Vitamin D (µg)	3.12±1.10	4.27±1.64	4.30±1.47	4.11±1.32	5
	62.40%	85.40%	86.00%	82.20%	
Calcium (mg)	681.50±30.24	898.85±41.27	899.66±36.27	896.45±35.87	1000
	68.15%	89.89%	89.97%	89.65%	
Iron (mg)	8.52±2.31	13.63±3.10	12.89±3.21	11.24±3.04	15
	56.80%	90.87%	85.93%	74.93%	
Zinc (mg)	7.23±2.40	9.21±1.90	9.16±2.01	8.63±1.62	12
	64.36%	76.75%	76.33%	71.92%	

RDA: Recommended daily allowance

regimen and the different types of diet consumed by the 3 groups of the obese women. The contents of calories, protein, fat and carbohydrate of the habitual diet were high compared to that of the three different regimens. The data showed the balanced and healthy distribution of the macro and micro-nutrients in the two regimens (fennel and chia) compared to the habitual diet. The analysis shows high contents of dietary fibers, vitamin A and D, calcium, iron and zinc of the two regimens (Fennel and Chia) especially that supplemented with fennel. Furthermore, it was clear from the

Table 5: Cognitive functions tests presented as percentage of obese women at basal and the end of dietary therapy

	Score (1)		Score (2)		Score (3)	
Variables	Basal	Last	Basal	Last	Basal	Last
Percentage of obese women						
MMSE	6	4.5	85	80.5	9	15
Appetite	5	6	20	51	75	43
Mood	35	11	58	79	7	10
Stress	15	23	50	47	35	30
Tea and coffee consumption	17	11	75	84	8	5
General activity	28	13	56	64	16	23
Exercising	49	32	46	62	5	6

*MMSE (mini mental state examination): 22-25 = 1, 26-28 = 2 and 29 = 3.*Mood: Bad = 1 , regular = 2 and good = 3. *Tea and coffee consumption (number of cups per day): 0-1 = 1, 2-4 = 2 and 5-8 = 3. The following variables were classified as, Stress, Appetite, General activity, Exercising: 1 = low, 2 = medium and 3 = high

Table 6: Mean±SE of age, anthropometric parameters and blood pressure among obese subjects at the basal and the end of the dietary therapy

	Group (A) (no. = 50)		Group (B) (no. = 46)		Group (C) (Control) (no. = 44)	
Parameters	Basal	Last	Basal	Last	Basal	Last
Ages (year)	49.82±1.31		51.60±1.02		48.21±1.58	
Height (cm)	156.59±0.84		157.20±0.96		156.93±1.30	
Weight (kg)	87.79±2.18	85.15±2.12**a	92.60±1.90	89.68±1.80**b	92.50±2.72	91.34±2.77
Change (%)	-3.00		-3.15		-1.25	
BMI (kg m^{-2})	35.78±0.81	34.70±0.78**a	37.52±0.78	36.34±0.74**b	37.58±1.05	37.10±1.05
Change (%)	-3.02		-4.43		-1.28	
BF (%)	47.83±0.76	46.94±0.77**a	49.11±0.71	48.12±0.70**b	48.64±0.86	48.01±0.87
Change (%)	-1.86		-2.02		-0.31	
LBM	43.22±0.61	40.63±1.70**a	45.29±0.78	44.88±0.77**b	44.74±0.87	44.49±0.87
Change (%)	-5.99		-0.91		-0.56	
MWC (cm)	97.09±1.43	91.87±1.44**a	102.81±1.64	98.30±1.64**b	97.94±1.98	95.21±1.95
Change (%)	-5.38		-4.39		-2.79	
Hip (cm)	120.72±1.68	116.67±1.63**a	124.59±1.64	120.46±1.43**b	126.18±2.44	123.18±2.33
Change (%)	-3.36		-3.32		-2.38	
WHR (cm/cm)	0.81±0.01	0.79±0.01**a	0.83±0.01	0.82±0.01*b	0.78±0.01	0.77±0.01
Change (%)	-2.47		-1.21		-1.28	
SBP (mmHg)	123.82±2.61	119.41±0.18**a	123.00±1.78	121.00±1.45**b	115.71±2.05	116.43±1.83
Change (%)	-3.56		-1.62		0.62	
DBP (mmHg)	73.53±1.86	70.59±1.40**a	73.75±1.50	71.00±1.12**b	65.71±1.20	66.07±1.16
Change (%)	-4.0		-3.73		0.55	

Change (%) BMI: Body mass index, BF (%): Body fat (%), LBM: Lean body mass, MWC: Minimal waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure. Significance: a: Basel obese group (A) vs. Last obese group (A) / b: Basal obese group (B) vs. Last obese group (B), *p<0.05 **p<0.01

table that the content of all elements of vitamin B increased in the different types of diets that consumed during intervention, compared to the habitual diet of the volunteers.

At the basal visit, almost all patients suffered from bad mood in more than 35% of the sample as shown in Table 5. After the dietary intervention, a satisfactory improvement in the cognitive functions as recorded by the mini mental state examination. The mood status, general activity, exercising and subjective reporting to feeling stressed were also improved.

Mean±SE of age, anthropometric and blood pressure measurements among obese subjects at the basal and after 8 weeks of following the dietary therapy were shown in Table 6. All the anthropometric parameters and the blood pressure values of the 2 groups (A and B) decreased significantly at the last visit, the percent decrease varied from -0.91-5.99%. While those of the control group showed only numerical decrease ranged from -0.31-3.04%. Both systolic and diastolic blood pressure of the control group showed numerical increase after the dietary therapy.

The Mean±SE of the different investigated biochemical parameters at the basal and last visits are shown in Table 7. Significant improvement in the hemoglobin, FBG and serum lipid profile values after the dietary therapy was recorded in both groups (A and B). The percent change was greater in group (A) consuming the supplement made from 10% fennel (ranges from 5.28-25.38%), compared to group (B) consuming the supplement made from 10% chia seeds (ranges from 6.36-20.41%). After the dietary therapy, the control group showed that the triglycerides and very low density lipoprotein (VLDL) decreased significantly (p<0.01), while fasting blood glucose (FBG) and the other parameters of the lipid profile decrease numerically. At the basal visit, the serum concentration of amyloid beta (Aβ), the biochemical marker of cognitive function impairment, was higher than the normal

Table 7: Mean±SE of biochemical parameters of the three groups at the basal and the end of the dietary therapy

	Group (A) (no. = 50)		Group (B) (no. = 46)		Control (no. = 44)	
Parameters	Basal	Last	Basal	Last	Basal	Last
FBG (mg dL^{-1})	110.09±5.26	90.44±2.30^{**a}	125.96±8.66	106.41±4.51^{**b}	120.69±7.92	105.73±3.27
Change (%)	-17.85		-15.52		-12.40	
TG (mg dL^{-1})	126.08±5.80	94.08±7.25^{**a}	148.68±8.86	118.34±5.70^{**b}	121.46±9.65	86.78±7.45^{**c}
Change (%)	-25.38		-20.41		-28.55	
VLDL-C (mg dL^{-1})	25.22±1.16	18.82±1.45^{**a}	29.74±1.77	23.67±1.14^{**b}	24.29±1.93	17.36±1.50^{**c}
Change (%)	-25.38		-20.41		-28.55	
TC (mg dL^{-1})	195.58±7.22	176.90±5.72^{**a}	191.71±3.53	178.92±3.01^{**b}	199.52±7.0	192.76±6.48
Change (%)	-9.55		-6.67		-3.39	
LDL-C (mg dL^{-1})	118.78±7.46	100.62±5.49^{**a}	111.07±4.28	100.64±3.38^{**b}	116.29±8.38	116.73±6.77
Change (%)	-15.29		-9.39		+0.37	
HDL-C (mg dL^{-1})	51.59±1.37	57.47±1.92^{**a}	50.90±1.99	54.62±2.05^{**b}	58.94±2.49	58.67±2.49
Change (%)	+11.40		+7.31		-0.46	
Non-HDL (mg dL^{-1})	143.99±7.02	119.43±5.23^{**a}	140.80±3.97	124.30±3.62^{**b}	140.58±7.98	134.09±6.38
Change (%)	-17.06		-11.72		-4.62	
Risk factor (TC/HDL-C)	3.84±0.14	3.14±0.12^{**a}	4.0±0.18	3.47±0.15^{**b}	3.60±0.22	3.41±0.15
Change (%)	-18.23		-13.25		-5.28	
Hb (g dL^{-1})	11.74±0.22	12.36±0,19^{**a}	12.43±0.19	13.22±0.19^{**b}	12.91±0.31	12.78±0.25
Change (%)	+5.28		+6.36		-1.0	
Amyloid β (pg mL^{-1})	659.25±40.26	517.30±47.95^{**a}	676.32±44.24	634.53±44.73	747.80±43.25	686.94±57.71^{*c}
Change (%)	-21.53		-6.18		-8.14	

FBG: Fasting blood glucose, TG: Triglycerides, VLDL: Very low density lipoprotein cholesterol, TC: Total cholesterol, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, Hb: Hemoglobin. Significance: a: Basal group (A) vs. Last group (A); b: Basal group (B) vs. Last group (B); c: Basal control (group C) vs. Last control (group C), *p<0.05 **p<0.01

range in the whole studied sample. After 8 weeks of dietary intervention, there was a significant decrease in Aβ level among group (A) (p<0.01) and the control group (C) (p<0.05), while only a numerical decrease was detected in group (B). The highest percent decrease was detected among group (A) (21.53%) compared with the 2 other groups.

DISCUSSION

Data of this study revealed that reduction of body weight either by consumption of low caloric regimen alone or by the low caloric regimen plus the two different supplements reduced the level of serum Aβ protein and improved the metabolic profile of the patients. However, the higher percent of reduction (-21.53%) in the concentration of serum Aβ protein was observed with the fennel supplement. In this context, Guo *et al.*[45] reported that maca was a newly known functional food. Maca root (*Lepidium meyenii*) is a member of the *Cruciferous* family, it could play an effective role in improving the cognitive function in mouse through up regulation of the autophagy-related proteins and through improving the mitochondrial function.

In the same time previous studies stated that plasma Aβ measures possibly aid in clinical investigations as markers for the pharmacological impacts of medications that influence amyloid protein (APP) transformation. For example, decreased plasma Aβ levels might affirm the effect claiming the medications that restrain β-secretase or γ-secretase that produces Aβ. Cross-sectional investigations found no critical impacts for statins, estrogen, non-steroidal anti-inflammatory drugs, antioxidants, alternately cholinesterase inhibitors on plasma Aβ levels[46-48]. On the other hand, alongside double-blind placebo-controlled studies, found that lovastatin decreased plasma Aβ levels over 3 months and transdermal 17β-estradiol might have been connected with a decrease of plasma $A\beta_{40}$ through eight weeks[49].

Diehl-Wiesenecker *et al.*[50] reported that central adiposity have been associated with expanded danger for AD. Visceral fat tissues have different metabolic aspects which were associated with AD when compared to subcutaneous fat. Data of this study showed that the high percent decrease of the chest circumference, minimal waist circumference (MWC) and waist hip ratio (WHR) (denoting central obesity) was reported in group (A) that followed regimen supplemented with fennel which matched with the higher percent decrease in the level of Aβ protein in the same group.

One of the advantages of fennel was accounted for by Bae *et al.*[51], where they stated that drinking the Fennel tea and fenugreek tea were essentially viable guides to curb the subjective hunger among the overweight. Moreover, a portion of the distributions expressed that *F. vulgare* has a unique sort of memory-improving effect[52].

Experimenting with laboratory animals and few clinical human cases indicated that it's safe to use the herb. One can also eat it on a regular basis either raw or cooked in any form such as stewed, boiled, grilled, or baked, or even drank as herbal teas or spirits. Therefore, incorporating fennel in a diet would be very beneficial health wise due to its richness in essential fatty acids[53].

Increased serum plasma cholesterol levels have been claimed to be a hazard figure for acquiring AD[54], moreover, there are issues with that speculation[55,56]. An adjustment of that speculation was the idea that high serum cholesterol levels amid middle aged were connected with an imminent danger of AD[57]. Metabolic burdens including dysglycemia, corpulence and hepatic steatosis could be basic to Aβ aggregation at the early phase of AD[58]. In this study, the higher percent reduction in the levels of the glucose, TC, LDL-C, non HDL and the cardiovascular risk factor and the higher percent increase in the concentration of HDL-C were observed with the patients consumed the fennel supplement and these matched with the percent decrease in the level of serum Aβ protein. It has been reported that fennel has antioxidant, antitumor, chemopreventive, cytoprotective, hepatoprotective, hypoglycemic and oestrogenic activities[59,60].

Li *et al.*[18] demonstrated that in healthy elderly Aβ concentration was correlated with cognitive functions in a state like early Alzheimer disease.

Ogawa[61] expressed that a low cognitive state is the result from a deficient diet and hence a kind of malnutrition. Prospective[62] and case-control studies[63,64] have demonstrated that low dietary intake of B vitamins was connected with intellectual decrease, or an impending danger of contracting AD. In this specific situation, the level of B vitamins in blood, particularly folate, was influenced by dietary intake[65].

Data of this study revealed improvement of all the cognitive function parameters of the oral tests with decrease in the concentration of the serum Aβ protein that might be a result of improvement of biological conditions, body weight reduction that accompanied dietary therapies. In addition, improvement of diet constituents after intervention represented by the decrease of calories and the improvement of the level of minerals as calcium, zinc, iron and vitamins especially vitamin A, B and D were recorded. In addition, this data suggested that measurement of the levels of serum amyloid β protein can aid in the identification of cognitive functions decline and may be used as a biochemical marker in such condition.

CONCLUSION AND FUTURE RECOMMENDATIONS

It was concluded that there was a close relation between middle age obesity and cognitive functions impairment. Using dietary therapy that consists of hypocaloric regimen and supplements contain bioactive components proved to be effective in ameliorating such a condition. Fennel (*Foeniculum vulgare*) has emerged as a good source of local traditional medicine. In this study, fennel showed better health effects and may be an effective functional food for slowing down age-related cognitive decline compared to the supplement containing chia seed (*Salvia hispanica*).

Additional studies are needed to demonstrate the effect of obesity on cognitive functions, its mechanisms, related biomarkers to predict changes in cognitive functions and defining better tools for diagnoses and follow up.

SIGNIFICANCE STATEMENT

This study revealed the importance and the healthy beneficial effect of using different functional foods in the form of dietary supplements as a preventive strategy to reduce the incidence of dementia later in life. Proper management of obesity in the middle age will help to reduce complications later in life including dementia pandemic.

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