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Melatonin the sleep hormone: could it be a future potential for the management of human obesity?

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Abstract

The pineal melatonin hormone is crucial for controlling the circadian cycle, mood swing, sleep quantity, quality and pattern. Postmenopausal females frequently complain of weight gain, body fat accumulation, increase waist circumference, and sleep disturbance with frequent nocturnal awakenings and difficulties initiating sleep. The aim of this study was to study the correlation between serum melatonin hormone level and response to diet therapy in postmenopausal Egyptian obese females. We prepared a food supplement in the form of crackles prepared from corn flour, wheat germ, flaxseed oil and enriched with clove and cinnamon powder. The chemical composition analysis of the crackles revealed that they were rich in healthy fat, fibre and protein. The subjects were classified into the groups according to the serum melatonin level; group (A) has serum melatonin value less than 5pg/ml, while group (B) has morning melatonin ≥ 5pg/ml. After six weeks of diet regimen protocol supplemented with daily consumption of 100 gram of prepared crackles by post menopausal obese women; there were statistical significance decrease in weight, BMI, %BF, waist and hip circumferences, total cholesterol level, and serum triglyceride. Moreover, the interleukin-6 as a marker of inflammation was decreased in both groups. There was statistical significant increase in serum HDL and total antioxidant capacity, while basal metabolic rate increased numerically without statistical significance. Studying the response to food supplements in weight reduction in relation to the morning serum melatonin level, we found that improvement was more in group with high melatonin level (≥ 5pg/ml) as regard measured parameters. The current study demonstrated that women whose melatonin level was high were more responsive to the diet therapy than women with low melatonin level. The results highlighting the potential benefit of exogenous melatonin during weight loss program in the postmenopausal obese women. It is promising to assess serum melatonin level in postmenopausal women to estimate the need to increase the intake of melatonin rich foods or melatonin tablets supplement in weight loss program.

Keywords: Melatonin hormone, Menopause, weight loss, body fat, metabolism, functional foods.

1. Introduction

Menopause marks the end of menstrual cycles in consequence of the decline in estrogen hormone secretion. Moreover, a lot of estrogen deficiency symptoms and metabolic problems emerge at menopausal phase of women's lives. Of these symptoms, hot flashes, night sweat, mood swing, vaginal dryness, increase in body weight, increase waist circumference, and insulin resistance. Obesity is the predisposing factor of ischemic heart disease, cerebro-vascular disease, renal disease, osteoporosis and tumors. [1]

World Health Organization (WHO) defines obesity as a state of chronic inflammation due to accumulation of fat. It is one of the most common co-morbidity associated with menopause; obesity is not only a medical health problem, but also an economic and social problem. The mechanisms and theories of

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the increase in body weight and obesity during menopause are not clearly elucidated. One of these mechanisms is a hormonal theory due to the rapid fall in estrogen levels and hyperandrogenemia, other theories include genetics factors and/or exogenous factors such as unhealthy foods and low physical activity. The end results are an increase in female body weight, an increase of fat mass mainly abdominal obesity and a decrease in fat free mass. [2]

Aging is linked with circadian rhythm impairment and decreases in melatonin hormone secretion from pineal body [3]. Serum concentrations of melatonin hormone secretion vary with age, its secretion decline gradually during middle age, and in old people its serum level are very low. The physiological functions of melatonin hormone include sleep wake rhythm, antioxidant actions, free radicals detoxification, neuroendocrine rhythms, bone protection, immune function, body temperature, brain and gastrointestinal protection, food intake and body mass regulation. [4]

Usage of functional foods in management of medical problems became essential last few years, keeping the market of functional food on expanding [5]. Cereals are one of the important foods in human nutrition; they can be used as raw material for obtaining flour for different baking products. The grass family includes wheat, rice, corn, oat, rye and barley [6]. Wheat is the most common cereal used across the world as a food ingredient, due to its capability to be ground into flour. Wheat germ, wheat bran and the endosperm represent about 25% of wheat milling output. Wheat germ is a nutritious raw material used in preparation of food product as snack foods, germ-enriched bread and breakfast cereals [6]. Corn or maize is an excellent source of fibre, which provide satiety feeling, prevent constipation and manage dyslipidemia. [7]

The aim of this study was to study the correlation between serum melatonin hormone level and response to diet therapy in postmenopausal Egyptian obese females, by assessment the effect of consumption of food supplement prepared from corn flour, wheat germ, flaxseed oil and enriched with cinnamon, and clove as regard the anthropometric and biochemical parameters.

2. METHODOLOGY

2.1. Study design

This study was conducted in nutrition and food sciences department, NRC in Egypt. It is an experimental study using purposive sampling method; based on previous study, representative sample was elected. The protocol of the study was approved by the Ethical Committee of NRC (Registration Number 16/110) and was in accordance with the principles of Helsinki Declaration; all participants provided written informed consent following a full explanation of the purpose of the study.

2.2. subjects:

Patients were recruited from menopausal females (with at least one year of last menstrual period), diagnosed by BMI as overweight or grade I obese individuals, ageing between 45 and 55 years, not suffering from diabetes mellitus, renal diseases, liver diseases, thyroid disorders, autoimmune diseases or psychological diseases. They were referred to Nutrition and food sciences department at NRC - Egypt for weight control. Subjects were excluded if they were consuming weight affecting medications including corticosteroids, weight loss prescriptions and antidepressants therapy. Participants were evaluated for anthropometrics measurements, 48-hour food recalls and relevant biochemical tests at first and last days of the study with weekly follow up.

2.3. Diet therapy

Subjects followed a low caloric diet prescribed to each subject according to her physical activity and food like habit. Caloric requirement for females was calculated by Harris Benedict equation, and then we subtracted 500 calories from the calculated energy requirement at first day and every two weeks. The subjects were informed to add complex carbohydrate to their diets, to consume fresh seasonal fruits and vegetables, to eat protein from different sources and to decrease consumption of junk foods, fried foods and bagged meats. In addition to consume 100 gram of prepared crackles/day as a snack for six weeks.

2.4. Anthropometrics and dietary recalls:

Participants' body weight, heights, waist circumference, neck circumference, hip circumference and body composition were measured by the same investigator. Waist circumference was measured at the narrowest level at the midpoint of the abdomen between the last rib and the iliac crest using a non-stretching tape. Body mass index was calculated using Quetelet's equation [8]. Body composition was assessed by Geratherm Body Fitness (B-5010) - German, to estimate the body composition concerning the lean body muscle mass, body fat percentage from the body weight, and resting basal metabolic rate. Dietary intakes recalls were analyzed using World Food Dietary Assessment

System (WFDAS, 1995); University of California, USA.

2.5. Biochemical analysis:

5 ml fasting blood samples were drawn at 8:30 AM from all subjects under complete aseptic conditions at first day and the last day of the study. The collected blood samples were left to clot and then centrifuged at 3000 rpm for 10 minutes, and then the sera were separated. Glucose and lipid biochemical tests were deliberated by Olympus AU400.

Serum Melatonin was determined by ELISA kits (SinoGeneClon Biotech Co., Ltd china) according to Kennaway [9] Catalog No:SG-10579 and expressed in pg/ml. The method employed in this kit is known as Sandwich-ELISA. The Microelisastripplate included in the kit comes pre-coated with an antibody that specifically binds to melatonin. To conduct the assay, standards or samples were added to the appropriate wells of the Microelisastripplate, where they interact with the specific antibody. Subsequently, a Horseradish Peroxidase (HRP)-conjugated antibody, which was specific to melatonin, was added to each well of the Microelisastripplate. The mixture was then incubated to allow the formation of the antibody-antigen-enzyme-antibody complex. After incubation, any unbound components were washed away. Following this, a TMB substrate solution was added to each well. Only those wells containing melatonin and the HRP-conjugated melatonin antibody had exhibit a blue color, which turned yellow upon addition of the stop solution to terminate the reaction. The optical density (OD) of the wells was measured spectrophotometrically at a wave length of 450 nm. The OD value obtained was directly proportional to the concentration of melatonin in the samples. By comparing the OD of the samples to a standard curve, the concentration of melatonin in the samples could be determined accurately. [10]

Total antioxidant capacity (TAC) which is the measure of the amount of free radicals scavenged, serum TAC Assays was assessed by a test solution [11], and was determined according to the colorimetric method of Koracevic et al. [12]. The assay measured the capacity of the biological fluids to inhibit the production of thiobarbituric acid reactive substances (TBARS) beneath the manipulate of the free oxygen radicals derived from Fenton's reaction.

Serum Interleukin-6 (IL-6) level was determined according to Chung et al.[13] using human ELISA reagent kits purchased from Sino Gene Clon Biotech Co., Ltd, Cangxin Road,Yu Hang District, Hang Zhou, China.

2.6. Crackles Preparation:

The crackles were prepared by mixing corn flour (60%), wheat germ (14%), full cream milk powder (10%), flaxseed oil (10%), clove powder (2%) and cinnamon powder (3%); then we added egg, baking powder and the suitable amount of water [14]. The crackles were baked at 180 °C in an electrical oven for about 18 minutes. Volunteers' subjects consumed 100 gram/day of the prepared crackles for 6 weeks.

Chemical composition (moisture, ash, crude protein, fat and crude fiber contents) were determined in raw materials and prepared crackles according to the methods outlined in A.O.A.C. [15]. Carbohydrates were calculated by the method of difference, according to FAO [16]. Color measurement determination in the prepared crackles was measured using Hunter Lab (Scan XE-Reston VA, USA).

Fatty acid methyl esters were prepared using Boron trifluoride methanol reagent according to Wirasnita and colleagues [17] for estimation of Relative percentages of fatty acid content in the crackles. The acid value (AV) of flaxseed oil sample was determined according to the method of AOCS, Cd 3a-63 [18]. Sensory evaluation of the prepared crackles was evaluated as described by Hussein et al. [19].

2.7. Statistical analysis

Statistical analysis of data was performed using the SPSS program version 16. Data were presented as mean ± standard deviation (SD) for parametric variables and percentage of total for categorical variables. Student's *t* test was used to compare quantitative data between the same group and between the two groups. ANOVA test was used to compare parameters between different groups. The Pearson correlation coefficient was used to measure correlations between melatonin and different quantitative variables. Differences were considered to be significant at $P < 0.05$.

3. RESULTS

The chemical composition of the dry ingredients and crackles was determined and presented in table (1). Corn flour was characterized by its higher carbohydrate content (65.95%), wheat germ contained high crude protein (32%), flaxseed oil was higher on fat content (37.54%) and the prepared crackles were good source of protein, fat and fibre.

Table (1): Chemical composition of raw materials and of the prepared crackles

Ingredients and crackles	Moisture %	Ash %	Protein %	Fat %	Fiber %	Total carbohydrate
Corn Flour	12.15±0.17	3.02±0.15	11.75±0.22	3.90±0.19	3.22±0.13	65.96±0.85
Wheat germ	11.50±0.10	4.74±0.19	32.00±0.30	9.37±0.06	2.12±0.09	40.27±0.65
Full Cream Milk Powder	2.69±0.12	4.55±0.22	22.11±0.36	3.02±0.19	-	70.32±0.72
Flax seed oil	6.46±0.16	3.12±0.15	20.17±0.11	37.54±0.29	6.37±0.10	26.34±0.33
prepared crackles	3.94±0.02	1.91±0.03	13.23±0.09	12.68±0.12	11.61±0.05	57.77±0.55

The data represented the mean ±SD of three replications.

Estimation of relative percentage of fatty acid contents in the prepared crackles revealed that it was rich in linoleic acid, linolenic acid and oleic acid as demonstrated on (table 2), acid value of flaxseed oil used in the preparation of the crackles was estimated 1.29 mg KOH/kg oil.

Table (2): Relative percentage of fatty acids contents in crackles

Fatty acids contents in crackles	Relative percentages
Palmitic acid (C16:0)	3.26
Stearic acid (C18:0)	1.61
Oleic acid (C18:1)	42.67
Omega 6 Linoleic acid (C18:2)	12.87
Omega 3 Linolenic acid (C18:3)	19.32
Arachidic acid (C20:0)	----

Data presented in (Table 3) showed that the sensory evaluation of the prepared crackles (color, flavor, taste and crispiness) was overall acceptable.

Table (3): Sensory evaluation of prepared crackles

Sensory evaluation	Appearance (20)	Colour (20)	Odour (20)	Taste (20)	Crispiness (20)	acceptability(100)
crackles	17.55±0.66	18.12±1.13	19.12±0.96	19.0±1.10	18.11±0.85	91.90±2.65

Table (4) showed the nutrition facts of the prepared crackles; the crackles were good source of polyunsaturated fat, fibre, vitamins and minerals with low saturated fatty acid content. The crackles were rich in magnesium, calcium, zinc, phosphate and iron.

Table (4): Nutrition facts of the prepared crackles per 100 gram

Constituents (%)	100 gram of crackles
Moisture	6.37
Energy (kcal)	384.11
Protein(g)	14.13
Fat (g)	12.99
Fiber fiber(g)	12.91
Total Carbohydrate(g)	57.92
SFA (g)	1.28
PUFA (g)	2.89
Cholesterol (mg)	2.6
Vit. A (µg)	56.18
Vit. D (µg)	0.5
Phosphorus(mg)	267.12
Potassium(mg)	362.52
Calcium (mg)	166.04
Magnesium(mg)	116.97

Sodium(mg)	6.91
Iron(mg)	3.8
Zinc (mg)	3.01

Analysed by Nutri-survey software 2007 – USA

Table (5) demonstrates the results of the analysis of the food intake at the first day of the study and six weeks later by World food analysis program. The percentage calorie supplied from carbohydrate, protein and fat of the diet containing the crackles were within the RDAs than the conventional diet, which provided high caloric intake from fat source. Moreover, the diet regimen contained more calcium, iron, potassium and zinc and less sodium content than in their conventional diet. The diet with crackles provided high fibre supply (24.76 g/day), which give sense of more filling than foods low in fibre content, staying satisfied long time which means subject consumed fewer calories per day without feeling hungry. In addition, they consumed polyunsaturated fatty acid 12.08 gram/day, monounsaturated fatty acid 14.93 g/d, saturated fatty acid 10.06g/day and cholesterol 235.06 mg/day which were within the RDAs.

Table (5): Daily intake of calories, macronutrients (% of calories), mean ± SD of the daily nutrients intake of conventional diet and of diet regimen with crackles supplement

Macronutrient intake	**Conventional diet**	**Diet regimen with crackles**
Energy (kcal)	2458.23±34.52 **	1196.90±25.23
Carbohydrate (%cal. Supply)	38.73%**	53.51%
Fat (% cal. Supply)	41% **	30.37%
Protein (% cal. Supply)	12.43% **	15.83%
Nutrient intake (RDAs)	**Mean ± S D %RDA**	
Dietary fibre (g) (25)	17.01±10.11 79.56	24.76±10.30* 99.04
Vit. A (µg) (800)	610.54±38.18 77.06	696.52±40.11 87.07
Vit. D (µg) (5)	2.11±1.05 39.20	3.90±1.17 * 78.00
Sodium (mg) (1500)	1643.32±22.32* 110.29	1158.77±21.35 77.25
Potassium (mg) (2000)	2239.82±32.61 111.39	1968.43±29.14* 98.42
Calcium (mg) (1200)	621.44±23.08 52.45	990.24±22.32* 82.52
Iron (mg) (15)	6.01±1.33 41.09	9.33±1.05* 62.20
Zinc (mg) (12)	6.38±1.12 53.07	7.69±1.13* 64.08

* Significant at $P \leq 0.05$ ** Significant at $P \leq 0.01$

The large number of subjects with obesity had the highest intake of sweets, pasta and bread, and low consumption of milk products, as demonstrated from percentage of the frequency consumption of different food matter summarized on (table 6).

Table (6): The percent of the frequency consumption of different food categories at the first visit for studied subjects

Items	Once/ daily	Two times / Day	Three times / Day	Four &more times / Day
Bread and bakery products% of Sample				
Bread	8.62	12.38	72.23	6.27
Bakery products	5.64	67.18	21.77	5.41
Pasta	89.48	5.60	3.69	1.23
Milk & milk products% of Sample				
Milk	32.12	63.57	3.27	1.04
Cheese	18.98	70.98	6.40	3.64
Yoghurt	36.97	59.90	2.03	1.10

Chicken ,meat & fish	Once / Week	Two / week	Three / week	Four &more /week
Chicken	6.22	46.45	39.41	7.92
Meat	14.32	62.57	20.81	2.30
fish	72.37	26.59	1.04	0.0
Egg	3.67	65.49	28.17	2.67
Legume	3.22	18.54	70.55	7.69
Vegetables & Fruits% of Sample				
Fresh Vegetables	1.13	7.23	10.67	80.97
Cooked Vegetables	1.01	10.33	65.39	23.27
Fresh Fruits	1.35	12.40	74.71	11.54
Fruit Juices	2.30	66.78	20.61	10.31
Sweet	0.0	12.40	73.38	14.22
Beverages% of Sample				
Tea	0.0	6.11	14.32	79.57
Carbonated drink	1.10	7.97	16.47	74.46

As normal average day time serum melatonin level is 5-50pg/ml [20], we classified the subjects into two groups according to the serum melatonin level, group (A) has morning melatonin value less than 5pg/ml with mean level 2.1 pg/ml and range (0.6- 4.1pg/ml), while group (B) has morning melatonin ≥ 5pg/ml with mean level 26.41 pg/ml and range (9.7-41.6 pg/ml).

The results of crackles consumption for six weeks on the anthropometrics, blood pressure and biochemical data were demonstrated in (table 7). Both groups were matching in all characteristics except for age and neck circumference. Subjects with melatonin level ≥ 5 had lesser neck circumference and were older age than the other group. Comparison of paired baseline and follow up values in both groups revealed that there were statistical significance decrease in weight, BMI, %BF, waist and hip circumferences, waist hip ratio, total cholesterol level, triglyceride, and interleukin-6. There was statistical significant increased in HDL and total antioxidant capacity, while BMR increased without statistical significance. Studying the percentage of change in both groups, we found that improvement was marked in group B with normal melatonin level as regard weight reduction, decrease in BMI, %body fat, hip circumference, WHR, systolic blood pressure, blood sugar and serum triglyceride levels, and improvement of BMR and HDL.

Table (7): Mean ± Standard deviation of relevant anthropometric and biochemical parameters of the participants at the basal and last visit of the study (total N =65)

Parameters	**Group (A) Serum melatonin <5pg/ml (n= 27)**			**Group (B) Serum melatonin ≥5pg/ml (n= 38)**		
	Basal	Last	%change	Basal	last	%change
Ages (year)	47.30±4.14		-	49.50±3.44		-
Melatonin(range) pg/ml	2.1 (0.6- 4.1)			26.41(9.7-41.6)		
Weight (kg)	85.06±7.98	81.89±7.97** a	-3.73	83.73±7.83	79.94±7.16**b	-4.53
BMI (kg/m²)	35.46±4.05	34.87±3.36* a	-1.66	34.25±3.72	33.08±2.98**b	-3.42
% BF	42.80±6.64	41.93±6.43** a	-2.03	41.20±5.98	39.91±6.12**b	-3.13
Neck circumference	37.57±2.60	37.11±2.78* a	-1.22	37.39±2.66	36.80±2.96**b	-1.58
WC (cm)	98.44±9,57	95.04±8.52**a	-3.45	98.24±8.23	94.44±7.01**b	-3.87
Body muscle mass	45.54±5.17	45.53±5.14	-0.02	45.55±5.93	45.54±5.91	-0.02
BMR	1977.52±189.18	1998.33±197.41	1.05	1993.55±174.66	2021.78±202.14	1.42
WHR (cm/cm)	0.84±0.01	0.78±0.01**a	-7.14	0.82±0.01	0.75±0.01**b	-8.54
Hip (cm)	122.24±10.58	118.33±9.85**a	-3.20	119.32±11.23	114.68±10.98**b	-3.89
SBP (mmHg)	115.93±14.08	111.11±12.81	-4.16	121.18±14.72	113.03±13.43	-6.73
DBP (mmHg)	69.63±13.08	67.78±11.38	-2.66	71.71±13.56	70.29±11.63	-1.98
FBS	104.52±21.40	106.22±14.71	1.626	108.0±21.87	103.89±19.44	-3.8055

Total cholesterol	199.76±28.82	185.03±28.20**a	-7.37	199.36±28.08	183.48±26.69**b	-7.97
TG	101.32±32.95	85.23±27.69**a	-15.88	101.34±30.13	81.96±29.68**b	-19.12
HDL	34.21±7.10	34.52±7.57	0.91	33.78±7.00	35.65±6.92*b	5.54
TAC	0.89±0.2	1.08±0.17**a	21.35	0.91±0.18	1.10±0.19**b	20.88
IL-6	55.56±8.71	28.15±3.81**a	-49.33	54.42±8.89	28.23±3.64**b	-48.13

BMI: Body mass index; %BF: % body fat percentage; LBM: Lean body mass; BMR: Basal metabolic rate; WHR: waist hip ratio;WC: waist circumference; WHR: waist hip ratio; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBS: fasting blood sugar; TG: triglyceride; HDL: high density lipoprotein; TAC: total antioxidant capacity; IL-6: Interleukin-6; *Significant at p<0.05; ** Significant at p<0.01; a: Comparison of paired baseline and follow up values in Group A; b: Comparison of paired baseline and follow up values in Group B.

Pearson correlation coefficient was studied in the studied groups between morning melatonin level and the different anthropometric and biochemical parameters; there was negative significant correlations between melatonin and % body fat (r: -0.232, $p = 0.001$), neck circumference (r = -0.264, $p< 0.001$), waist circumference (−0.276, $p< 0.001$), and IL-6 (r = -0.561, $p< 0.001$). While positive significant correlations was detected between melatonin and basal metabolic rate (r= 0.181, $p = 0.03$). Others anthropometrics parameters, glucose, TAC, lipid profiles and blood pressure were not found to have significant correlation with the morning melatonin level.

4. Discussion

There is no doubt that obesity has grown to be a challenging worldwide health disaster. Obesity is a chronic health condition that complicates over time and affects metabolic parameters. Post-menopausal women are predominantly complaining of obesity when compared to other human ages and sex groups [21]. After menstrual cycle cessation, there is an increase in percentage body fat and a decrease in lean body muscle mass. Currently, the management of postmenopausal obesity depends on healthy lifestyle modifications. However, the long term efficiency of these changes continuous to be a challenge, and the addition of pharmacotherapy is on the rise. [21]

Recommendation of consumption of functional foods is growing and will be an essential strategy for prevention and treatment of different diseases. Three types of functional foods are available in markets; conventional foods (such as vegetables, fruits and grains), modified food (foods fortified with specific nutrient) and the third category is the food ingredients enriched with fibers, phenols, and healthy fatty acids. [22]

Crackles were prepared from corn flour, wheat germ, flaxseed oil and enriched with clove and cinnamon powder. The crackles were rich in healthy fat, fibre and protein. After six weeks of daily consumption of the crackles by obese post-menopausal women; there were statistical significance decrease in the anthropometric parameters, total cholesterol level, triglyceride, and interleukin-6. There was statistical significant increase in HDL and total antioxidant capacity, while BMR increased without statistical significance. This could be explained by the satiety sense after consumption of protein and fibre high source foods. Studying the response to food supplements in weight reduction in relation to the morning melatonin level, we found that improvement was marked in group with normal melatonin level as regard weight reduction, control of BMI, %body fat, hip circumference, WHR, BMR, systolic blood pressure, HDL, blood sugar and serum triglyceride levels.

Decline of IL-6 and improvement of total antioxidant capacity after crackles consumption were good markers of health benefits of the dietary supplement in regulation of obesity; as IL 6 levels could be a marker for expectation of obesity complications and there is an inverse relationship between percentage body fat, central adiposity and body antioxidant capacity as concluded by El-Mikkawy and colleague [23]. Simopoulos and colleagues demonstrated that foods rich in ω-3 fatty acid have anti-inflammatory actions, while foods rich in ω-6 fatty acid leads to a state of inflammation, which is at the basis of obesity [24].

The 2017 Nobel Prize in Physiology Medicine is awarded to Jeffrey Hall, Michael Rosbash and Michael Young for their discoveries of molecular mechanisms that control circadian rhythms. Chronobiology is the study of the effects of time on biological events; it has a role in regulation of blood pressure, body temperature, sleep patterns, feeding behaviour, and endocrinal hormones release. [25]

Age is one of the factors affecting melatonin secretion; higher melatonin levels occur in children. A significant melatonin hormone secretion decline was observed in premenopausal females; different explanation was suggested, such as pineal gland calcification with degenerative changes of neurons of suprachiasmatic nucleus [26]. Greendale and colleagues declared that there is 30% diminution of melatonin secretion in postmenopausal females [27]. Another study concluded that in the menopausal women, serum melatonin median was 7.0 pg/ml [28].

Previous studies demonstrated that decrease endogenous melatonin levels strength sleep disturbances frequency in peri-menopause women [29-31]. They concluded that melatonin analogues

improve sleep quality and the vasomotor symptoms in these categories. Sleep disturbances triggers postmenopausal anxiety, depression, osteoporosis, generalized muscle pain and fibromyalgia, they advised in their study to use melatonin supplement, not only for substituting the hormonal deficiency, but also to recover the circadian system. [30-31]

Chu and colleagues concluded that serum melatonin measurement in postmenopausal women is a factor affecting cancer prognosis [32]. Recent research suggests that melatonin tablets can be used as a medicine to treat not only sleep disorders, but also for other medical purposes, such as cancer and neurodegenerative diseases [33].

Melatonin has an anti-inflammatory property; it inhibits the translocation of nuclear factor-kappa B to the nucleus, thus reducing the upregulation of cytokines, interleukins and tumor necrosis factor-alpha [34]. Sutton and colleague on 2022 demonstrated a decreased in the recurrence of Clostridioides difficile infection in patients receiving melatonin supplement denoting the beneficial property of melatonin as an anti-inflammatory and antibacterial in the gastrointestinal tract [35].

The connection between melatonin, overweight or obesity, and metabolic disorders has been studied in animal, while, few human studies have been conducted in this regard [36]. Melatonin, when released at night, it acts directly on the hypothalamus and inhibit hunger. Therefore, less melatonin secretion leads to an increase in the appetite, in addition, this causes an increase in lipid accumulation in adipose tissue.

This study focuses the attention of role of melatonin in regulating weight loss in postmenopausal obese subjects especially in percentage body fat loss, decrease in hip circumference, decrease in waist hip ratio and improvement of basal metabolic rate. Although there is no clinical evidence that recommend melatonin as an anti-obesity drug, but its role as anti-inflammatory, antioxidant, in regulation of dyslipidemia, gut microbiota, and sleep disorders, formulate melatonin as a hopeful manager to unlock new avenues in the management of obesity-related symptoms. This results were in agree with Guan et al. [37] and Rafael et al.[38].

Suriagandhi and colleague demonstrated that leptin secretion depends on melatonin level and circadian rhythm; leptin resistance leads to obesity due to excess food consumption and less energy expenditure. [39]

In humans, melatonin supplementation for sleep disorders is safe, and has no side effects reported within the dosages investigated [40]. Meng and colleagues recommended consumption of eggs, fish, nuts, mushrooms, germinated seeds cereals as high food sources of melatonin [41]. Efforts are in progress to develop approaches in pharmacology to adjust circadian rhythm clocks to recover human health [42].

5. Conclusion

Handling of functional foods to deal with postmenopausal obesity succeeded in reducing weight and improving metabolism, the metabolic profile and the inflammatory state of the obese subjects. The data obtained in this study give attention to the importance of serum melatonin level in management of obesity in postmenopausal females. The current study showed that women whose melatonin level was high were more responsive to the diet therapy. Melatonin prescription can be considered a promising mediator to open new avenues in the management of obesity.

6. Conflicts of interest

We have no conflicts of interest to disclose or to declare.

7. Formatting of funding sources

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8. Acknowledgments

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9. Ethics approval

The National Research Centre's Ethical Committee approved the research protocol with ID: 16/110. Each volunteer woman was required to sign a written informed consent form after being fully informed about the study's purpose.

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