Evaluation of safety and efficacy of Labeesity® 125mg for weight management and fatigue in university employees; a case report

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Abstract

There is a dramatic increase in the trend of obesity universally, thus the health and economic burden associated with obesity have become an important public health issue. The needs for the replacement of current drugs have turned the general public's attention to natural products assuming these to be as effective and safe antiobesity drug alternatives. In this study, we aimed to evaluate the efficacy and safety administration of Labeesity® 125mg, an antiobesity natural product supplement available on the market. A clinical obese female with medication-controlled hypothyroidism volunteered for this trial. The patient supplemented with Labeesity® 125mg twice daily for 40 days. The hematological, serum biochemical, subject characteristic was recorded before and after treatment.

When compared with the baseline reading, the treatment was favorable for weight loss, hip, and waist circumference reduction. It also improved the patient's general quality of life over the course of 40 days. There was no treatment-related negative clinical symptoms except for mild bloating which dissipated after the second week of supplementation. Furthermore, there were no significant hematological and biochemical alterations, except for a slight fluctuation in uric acid. Labeesity® 125mg intake for the volunteer is assumed to be generally safe with moderate improvement in weight reduction, body composition, and serum lipid profile. A longer period of observations on the effects of Labeesity® 125mg would be required to evaluate if the positive effects were seen would persist beyond 40 days of intervention. Therefore, strong evidence to support the potential effectiveness and long-term benefits of Labisia pumila extracts based products will require robust studies to be conducted utilizing larger patient numbers and over extended periods of time to rule out any potential toxic effects.

Introduction

The global increase in numbers of obesity among all populations and age groups has resulted in a significant increase risk of cardiovascular-related mortality and morbidity. Obesity is associated with elevated risk of cardiovascular disease, insulin resistance, dyslipidemia, metabolic syndrome, polycystic ovarian [1]. According to world health organization obesity is defined as an excess of body fat and defined by body mass index and waist circumference [2]. Body mass index, waist circumference, body and fat percentage are standard obesity indices for cardiovascular disease [3]. Pervious study showed high body fat percentage is a risk factor for both normal and low-BMI Asian population, despite the normal body weight [4]. Increased body fat occurs as result of many biological, hormonal, and behavioral patterns [5]. Apparently, dyslipidemia as characterized by low high-density lipoprotein cholesterol (HDL), and elevated low-density lipoprotein cholesterol (LDL), cholesterol and triglycerides play major role in accumulation of fat [6-8]. These aberrations consequent in metabolic disorder, proinflammatory condition, and hypertension, all risk factors for risk of cardiovascular disease [5]. Recently study showed regulation of dyslipidemia decreases morbidity and mortality of cardiovascular disease among adult Chinese [9]. Significant reduction in body fat correlates with managed dyslipidemia in human [10]. Currently, the use of available pharmacologic agents to control lipid disorder in the market is costly and not devoid of serious side effects [11]. The needs for the replacement of current drugs, has turned sufferers' attention to natural product as a potential source for a more effective and safer antiobesity drugs alternative.

Labisia pumila var. *alata* (LPva) (Primulaceae) is a plant commonly found in Southeast Asia and known as Kacip Fatimah. It has been used traditionally for maintenance of general health and vitality of female reproductive system. It has been a remedy for regulating menstrual disorders, postpartum complications, pre and post-menopausal symptoms as well as weight management [12-15]. LPva has been shown to exhibit pharmacological properties such as anti-photoaging [16] antioxidant [14, 17-19], anticancer [14] and anti-inflammatory [20], antimicrobial and antifungal [21-23] cardioprotective [24,

25] upregulation T helper1 [26], selective inhibition of CYP2C isoforms [27], antistress and adaptogenic potential [28]. LPva regulate metabolism via regulation of insulin sensitivity and lipid profile further by estrogenic effect evidenced by increased uterus weight [29]. Another study confirmed such an effect showing improved serum lipid profiles and modulation of serum antioxidants [30]. The extract and its isolated active compound gallic acid showed suppressed formation of fat droplets and triglyceride accumulation. In the study, gallic acids induced anti-obesity effect via inhibition of leptin secretion, triglyceride, LDL, VLDL, and promotion of HDL in an obese animal [31]. LPva extract consumption improved lipid profiles of pre- and postmenopausal women by regulation of total cholesterol as well as attenuating the effects of oxidative stress and inflammation. The consumption of the extract is assumed to be safe for postmenopausal women [32].

There is still very little information or clinical data on the safety of LPva for human consumption and medical applications. In a recent animal safety study, no treatment-related and mortality was reported in response to sub-acute oral toxicity aqueous extract of LPva (50, 250, 500, and 1000 mg/kg), while there were some toxicological concerns, evidenced by histopathological changes. These findings may suggest that aqueous extracts of LPva up to 1000 mg/kg/day statistically did not show any significant teratogenic effects in rats but it did dose-dependently affect the maternal body weight in animals receiving low dose extracts (2 mg/kg/day) [33]. Another study reported aqueous extract of LPva posed no significant toxic effect when tested on the estrous cycle, reproductive performance, post-natal growth and offspring survival of rats [34]. Subcutaneous administration of petroleum-ether extract of LPva (0.025, 0.05, and 0.1 mg/ml) induced organ toxicity evidenced by degeneration in sinusoid area in liver and glomerulonephritis and nephrosis of the kidney [35]. Leaves extract of LPva contain flavonoids such as quercetin, myricetin, kaempferol, naringin, rutin, apigenin, anthocyanins, catechin, epigallocatechin, and anthocyanins [18, 21, 36-38]. Phenolic acids; salicylic acid, syringic acid, vanillic acid, protocatechin acid, gallic acid, coumaric acid, caffeic acid, chlorogenic acid, and pyrogallol, ascorbic acid and β-carotene [18, 21, 36, 37] saponins [21, 39], and fatty acid [40].

The present study assessed the responses of a single female subject to 40 days intake of Labeesity® 125mg, Labisia pumila standardized extract. The specific goals were to evaluate the safety and effect of the test sample on weight management and fatigue. Patients' testimonies provided by the manufacturer indicate that the consumption of the standardized extracts in capsule form was associated with reports of general wellbeing, body weight, and fat loss. Nevertheless, caution on interpreting the results is exercised, as randomized, placebo-controlled clinical trials have not been carried out. There were also no records of any safety data such as blood test results measuring effects on liver function and renal function.

Methods

Labeesity®

A patent pending (Patent No. WO 2016093692 A1) 100% natural herbal extract made from Standardized Kacip Fatimah Extract (SKF7™) with each capsule containing N.L.T 4.5% gallic acid. Labeesity® 125mg is a recently marketed product by Orchid Life Sdn Bhd approved by Malaysia National Pharmaceutical Regulatory Agency (NPRA) with registration number MAL16125022TC. Labeesity® 125mg capsules were analyzed for microbial and heavy metal content prior to the commencement of studies.

Pretreatment and follow-up studies

Subject

The subject was a 59-year-old female university lecturer with a medical background of hypothyroidism on 100 mg thyroxine for 5 years. The subject was assessed to be clinically obese when volunteered for this study. She was confirmed not to be on any extraordinary weight management dietary program in the past or during the inclusion phase. After obtaining full informed consent to participate in the study, the subject was requested to maintain her regular diet and activities throughout the study period. Any deviations from her daily routine caloric intake or physical activities were recorded in a study diary.

Labeesity® dosage and schedule

The subject consumed Labeesity® 125mg 2 capsules, twice daily for 40 days, after meals i.e. after breakfast and after dinner. The 125mg capsule is chosen, as it is the standard recommended dose for the product in the market. The patient was then monitored fortnightly throughout the study period i.e. from (20/11/2016 to 6/1/2017).

Baseline and terminal assessment

The subject initially underwent general medical assessment; data were collected on blood pressure, heart rate, baseline anthropomorphic assessment, weight, body mass index (BMI), percentage body fat as well as blood and biochemical assessment at Quest International University, Perak, school of Medicine Clinic/Laboratory. All assessments were carried out within one clinic session prior to and shortly after completion of the study period. The patient was assessed at baseline using an investigator delivered patient-reported outcome assessment i.e. Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-Fatigue) to evaluate any difference in fatigue and general well-being.

Statistical analysis

Statistical analysis was conducted using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristic

The patient characteristics are detailed in Table 1.

Body composition

The results of measurement before and after 40 days treatment shows the subject with the BMI of 33.2 Kg/m^2 is identified as class one obese in lower cutoff point (32.50 - 34.99 Kg/m^2). After administration of Labeesity® 125mg, the subject experienced 2.51% decrease in body weight (90.5 vs. 88.2 Kg). These reduction results in BMI of 32.40 Kg/m^2, which is in the upper cutoff point (30.00 - 32.49

Kg/m^2) of class one obesity categories. There was a respectively 2.5 % and 2.95 % decrease in waist and hip circumferences. At the end of treatment with Labeesity® 125mg, 9 % decrease was observed in total body fat (Table 2).

Safety analysis

The patient generally did not experience any treatment-related adverse event during and by the end of intervention except for some mild sensation of bloating and gas which lasted during the first week of treatment commencement. There were no significant deviation in the full blood count and other hematological indices. The renal profile and liver function test also showed no apparent adverse effects or derangements in key biochemical markers except for the significant rise in uric acid ($P < 0.05$) (Appendix 1-Table 2). Full laboratory report on blood parameters and other biochemical profiles taken prior to consuming Labeesity® 125mg and after the last dosage were within average population reference range (Appendix 1).

Lipid profile

Significant deviations from baseline parameters in the lipid profile as well as uric acid were noted following 40 days of study initiation (Table 3). The result shows subject experienced significant ($P < 0.05$) decline in in total cholesterol, triglycerides, LDL – cholesterol, total Chol/HDL-Chol, uric acid by the end of treatment period. It further shows the HDL- cholesterol is significantly ($P < 0.05$) improved by Labeesity® 125mg administration.

Fatigue index

The FACIT-fatigue scale was measured before and after treatment. All negatively expressed items (e.g., I feel listless), showed lowered score, while the positively worded items (e.g., I have energy) showed the higher score. Compared to baseline response, there was an improvement of the total score of all items from 34 to 48. Except for general feeling of fatigue, which was same prior and after treatment, there was an improvement in all other items. The subject felt less tired and more energetic. She was capable of performing her daily activities with greater stamina, without frustration and need of

a daily nap. The subject also was able to participate in her usual active work and social activities.

Discussion

Overall, the subject reported significant improvement on many aspects of her quality of life. The subject had also reported and overall improvement based on FACIT-F scores after consuming the product. Although weight loss was not relatively prominent over 40 days, but there was nevertheless an improvement in BMI from lower cutoff point to upper cutoff point of class one obesity. There were significant decreases in body measurements i.e. waist and hip circumferences. A significant decrease in percentage body fat was also noted. All these together show there was a remarkable decrease in obesity index of the patient after 40 days. It is also noteworthy that there were significant improvements in all parameters of lipid profile. Significant reduction in LDL and Total Chol/HDL-Chol ratio was also noticed. It is also clear from subject's blood laboratory investigations there were no significant deviations in blood and biochemical parameters including liver and renal profile after 40 days on Labeesity® 125mg. It was noted that uric acid was mildly raised from the previous baseline. However, it is difficult to interpret if this small rise is related to the test article or a physiological response to its effects on cellular metabolism. The antiobesity mechanisms of LPVa in human and laboratory animal were mainly attributed to improvement of serum lipid profile, regulation of insulin sensitivity, attention of oxidative stress, and inhibition of leptin in obese model [29-32]. Labeesity® 125mg plays role in regulation of cardiovascular indices such as atherogenic dyslipidemia and factor such as BMI, WC, HP, and BFP, that related to central obesity. Based on these finding it is postulated that Labeesity® 125mg intake may be beneficial for a subject with the high risk of cardiovascular disease, hypertension, and insulin resistance. As the previous study showed regulation dyslipidemia decreased the risk of metabolic disorder and cardiovascular disease [10].

Gallic acid rich Labeesity® 125mg induced weight loss possibly via activation and modulation of the angiogenesis cascade in fat tissue. Gallic acid, a phenolic entity identified in different preparations of LPVa, has been reported to exert a notable antiangiogenic activity in animal model [41]. Modulation of

antiangiogenesis thus has been recently proposed as a potential pharmacological target for anti-obesity and weight management in human after success in preclinical models [42, 43]. With regard to toxicity and safety, it is important to note that except in rare cases, studies conducted in experimental animals have not reported increased mortality or significant toxicity in humans. The dose administered to the human volunteer in this study is well below the NOAEL in animals of 50 mg/kg and as such, there were no observed or reported adverse or side effects. A phase 1 pilot study is nevertheless required to establish a proper dose response relationship as well as evaluating a range of dosing regimens to determine the most efficacious and safe dose of the product. In summary, this case study indicates significant antihyperlipidemic activity of Labeesity® 125mg in 59 years old clinically obese women. The treatment was favorable for weight loss, hip, and waist circumference reduction. It also improved the quality of life of the subject over the course of 40 days. Labeesity® 125mg intake in this study can be assumed to be safe with no major record of treatment hazards throughout the intervention and no significant hematological and biochemical alteration, except for the slight modification in uric acid. It is difficult to say, however, whether the effects of Labeesity® 125mg would persist beyond 40 days of intervention. Therefore, strong evidence to support the potential effectiveness and long-term benefits of Labisia pumila extracts based products will require robust studies to be conducted utilizing larger patient numbers and over extended periods of time to rule out any potential toxic effects.

Table 1. Patient's baseline characteristics

Item	Unit	Reading	Category
Gender		Female	
Age	Years	59	(>18 and < 65 years)
Race		Malaysia Indian	
Occupation		University lecturer	
Height	m	1.65	
Weight	Kg	90.5	
BMI	Kg/m2	33.2	Class 1 obese
Waist circumference	cm	103	
Hip circumference	cm	120	
Body fat	Percentage	49 %	
Blood pressure	mmHg	135/67	
Heart rate	BPM	85	

Table 2: Body measurements before and after consuming Labeesity® 125mg

Item	Unit	Before	After	Percentage change
Height	m	1.65	1.65	0 %
Weight	Kg	90.5	88.2	2.51%
BMI	Kg/m^2	33.2	32.4	-
Waist circumference	cm	103	100	2.95 %
Hip circumference	cm	120	117	2.5 %
Body fat	%	49 %	40 %	9 %

Table 3. Serum lipid profile before and after consuming Labeesity® 125mg

Lipid profile	Unit	Before	After	Normal range
Total cholesterol(mmol/l)	(mmol/l)	5.28	*4.82	<5.18
Triglyceride (mmol/l)	(mmol/l)	2.01	*1.97	<1.7
HDL (mmol/l)	(mmol/l)	1.1	*1.2	>1.0
LDL(mmol/l)	(mmol/l)	3.3	*2.8	< 2.6
Total cholesterol /HDL ratio	-	4.9	*4.1	Risk indicate if > 4.5

Appendix 1

Table 1. Hematological parameters before and after administration of Labeesity® 125mg

Hematological parameters	Unit	Before	After	Normal range
Hemoglobin	(g/dl)	12.8	12.6	11.5-15.5
Total Red Blood Cell	(10^{12}/l)	4.4	4.3	4-5.5
Total White Blood Cell	(10^{9}/l)	9	9.2	4-11
Polymorphs	(%)	61	52	50-70
Lymphocyte	(%)	32	38	20-40
Monocyte	(%)	4	8	< 6
Eosinophil	(%)	3	2	< 4
Basophil	(%)	0	0	Less than 1
Mean Corpuscular Volume	(fl)	89	88	82-98
Mean Corpuscular Hemoglobin	(pg)	29	29	27-33
Mean Corpuscular Hemoglobin Concentration	(g/l)	33	33	31-35
Platelet Count	(10^{9}/l)	364	345	150-400
Red cell distribution width		12.2	12.7	11-16

Table 2. Serum biochemical parameters before and after administration of Labeesity® 125mg

Biochemical parameters	Unit	Before	After	Normal range
Total Protein	(g/l)	6.8	6.8	6.4-8.3
Albumin	(g/l)	3.7	3.8	3.5-5.2
Globulin	(g/l)	3.1	3	2.1-4.0
Albumin / globulin ratio		1.2	1.3	1.0-2.2
Total Bilirubin	(µmol/l)	0.8	0.8	0.2-1.2
Alkaline phosphatase	(U/L)	81	84	40-150
SGOT[a]/Aspartate aminotransferase	(U/L)	17	17	5-34
SGPT[b]/Alanine aminotransferase	(U/L)	14	16	0-55
Gamma glutamyl transferase	(U/L)	13	12	9-36
Potassium	(mmol/l)	5.1	4.5	3.1-5.1
Sodium	(mmol/l)	143	142	135-145
Chloride	(mmol/l)	108	106	98-107
Urea	(mmol/l)	3.3	3.2	3.0-9.2
Creatinine	(µmol/l)	61.9	64.5	50.4-98.1
Uric acid	(µmol/l)	393	*410	150-357

[a]: Serum glutamic oxaloacetic transaminase

[b]: Serum glutamic-pyruvic transaminase

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