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ORIGINAL ARTICLE

Long-term effects of consumption of a novel fat emulsion in relation to body-weight management

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Objective: To assess weight maintenance after weight loss by consumption of yoghurt with a novel fat emulsion (Olibra) including effects on body composition, resting energy expenditure (REE), fat oxidation, hunger feelings and satiety hormones.
Design: A randomized, placebo-controlled, double-blind, parallel design. A 6-week weight loss period (2.1 MJ/day) was followed by 18 weeks weight maintenance with test (Olibra) or placebo yoghurt.
Subjects: Fifty overweight women (age: 18–58 years, body mass index (BMI) 25–32 kg/m^2).
Measurements: In weeks 1, 7 and 25, a satiety test with questionnaires and blood samples for analysis of satiety hormones. In weeks 2, 8 and 26, REE, body weight and body composition.
Results: During weight maintenance after significant body weight reduction, there was no significant increase in body weight in the test group (1.1 ± 3.4 kg); the placebo group did gain weight (3.0 ± 3.1 kg, $P<0.001$). Compared to the placebo group, the test group was less hungry 4 h after yoghurt consumption in week 25 ($P<0.05$) and showed increased glucagon like peptide-1 values 180 min after yoghurt consumption (week 25 vs week 1, $P<0.05$). Measured REE as a function of fat-free mass (FFM) was significantly higher than predicted REE ($P<0.05$) in week 26 for the test group, but not for the placebo group. Fat mass (FM) was significantly more decreased in the test group (6.5 ± 4.1 kg) compared to the placebo group (4.1 ± 3.6 kg) (week 26 vs week 2, $P<0.05$).
Conclusion: Consumption of Olibra yoghurt improved weight maintenance compared to placebo, which can be explained by the relatively higher REE as a function of FFM, relatively higher decrease in FM and the relatively lower increase in hunger.
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Keywords: fat; emulsion; weight maintenance; body composition; resting energy expenditure; satiety

Introduction

The prevalence of obesity has increased worldwide during the past few decades.[1] Obesity is a major causative factor for a number of diseases, including coronary heart disease, hypertension, non-insulin-dependent diabetes mellitus, pulmonary dysfunction and certain types of cancer.[2] Obesity develops when the equilibrium between energy intake (EI) and energy expenditure (EE) shifts towards a positive energy balance.

Treatment of obesity is beneficial in that weight loss reduces the risk for mortality and morbidity. Even modest weight loss, such as 5–10% of the initial body weight, has beneficial health effects.[3,4] Body weight loss and prevention of body weight (re)gain can be achieved by reducing EI and/or increasing EE, or promoting fat oxidation.

Previously an Irish research group showed that, in comparison with a yoghurt containing only dairy fat, consumption of a 200 g yoghurt containing a novel fat emulsion (Olibra) significantly increased satiety and subsequently decreased EI in non-obese, overweight and obese subjects, at a meal 4 h later, and that the decreased intake persisted for the rest of the day.[5–7] This novel fat emulsion consists of a mixture of fractionated palm oil (40%) and fractionated oat oil (2.5%) in water, whereby 5 g of emulsion corresponds to about 2 g of fat. Until now, a possible long-term effect of Olibra has not been assessed. This study was executed in order to investigate the long-term effect of Olibra, and to improve understanding of the possible mechanisms underlying the observed short-term reduction in EI owing to Olibra consumption. Primary end points of the study were to assess possible weight maintenance (after a

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very-low-energy diet) by consumption of Olibra up till 18 weeks including effects on body composition, fat oxidation and resting energy expenditure (REE). Furthermore, hunger feelings as well as satiety-related hormones after consumption of an Olibra-containing serving were assessed.

Methods

Subjects

Fifty female overweight subjects, aged 18–58 years and with a body mass index (BMI) between 25 and 32 kg/m^2 participated in this study. The subjects were recruited by advertisements in local newspapers. All subjects participated in an initial screening that involved measurement of body weight, height, waist/hip circumference and completion of a questionnaire related to health, use of medication, smoking behavior, alcohol consumption and physical activity. All subjects were in good health, non-smokers, not using medication and at most moderate alcohol users. The subjects were stratified for age, BMI, weight, height, waist and hip circumference in two groups which were randomly assigned to the two treatments: the test treatment (Olibra, $n=22$) and the placebo treatment ($n=28$). Baseline characteristics of the subjects are presented in Table 1.

The subjects gave their written informed consent and the Medical Ethical Committee of Maastricht University approved the study.

Experimental design

The study followed a randomized, placebo-controlled, double-blind, parallel design and lasted 26 weeks. Subjects were instructed to maintain their normal physical activity level during the whole study period.

Measurements took place in weeks 1, 2, 7, 8, 25 and 26. In week 1, subjects came to the laboratory for a satiety test (hormones, hunger and satiety questionnaires) and determination of free fatty acids (FFA), triglycerides (TG), glycerol (Gly) and β-hydroxybutyrate (BHB). This test is described below. During 3 days before the next measurement in week 2, the subjects consumed a standardized energy balance diet (energy% C/P/F: 53/12/35) at 100% of predicted EE.[8] All food was supplied to the subjects. Anthropometry and REE were measured in week 2. During the following 6 weeks (weeks 2–8), the subjects consumed a very-low-energy diet (VLED) (Modifast, Novartis Nutrition, Breda, The Netherlands). This Modifast diet provided 2.1 MJ/day (energy% C/P/F: 42/44/14) and was supplied in three sachets daily, dissolved in water to obtain milk shake, pudding, soup or muesli. Subjects were instructed that vegetables and two pieces of fruit per day were allowed in addition to the VLED. Subjects could phone when they had remaining questions. The weight-loss-related measurements followed in weeks 7 and 8. These were the same measurements as during weeks 1 and 2. During the subsequent 18 weeks (weeks 8–26), the subjects stopped the VLED and entered the weight maintenance phase. The subjects resumed their habitual eating patterns during the weight maintenance phase and obtained either test (250 g yoghurt containing 3 g milk fat and 2 g vegetable fat, provided by 5 g Olibra emulsion (Lipid Technologies Provider AB, Karlshamn, Sweden)) or placebo yoghurt (250 g yoghurt containing 5 g milk fat) for daily use. Subjects were instructed to use 250 g in the morning (breakfast time) and 250 g in the afternoon (around 1600 hours) to aim at a possible decreased food intake at lunch as well as at dinner after consumption of the test yoghurt. Food intake compliance for yoghurt was evaluated every week by a personal interview by the dietician. The composition of both yoghurts was matched for energy and macronutrient content. Yoghurt consumption (500 g) provided 2.0 MJ/day = 476 kcal/day (406 kJ/97 kcal per 100 g, energy% C/P/F: 69/12/19). In weeks 25 and 26, the weight maintenance measurements followed. These were the same as during weeks 1 and 2.

Table 1 Subject characteristics at baseline

	Test group (n = *22*)	*Placebo group* (n = *28*)
Age (years)	40.3 ± 9.7	41.2 ± 9.3
Weight (kg)	81.3 ± 8.6	79.0 ± 8.6
Height (cm)	167.6 ± 7.8	166.3 ± 7.4
BMI (kg/m^2)	28.9 ± 1.7	28.5 ± 2.2
Waist circumference (cm)	91.1 ± 5.6	91.5 ± 7.7
Hip circumference (cm)	108.8 ± 4.3	108.1 ± 7.1
Waist/hip ratio	0.84 ± 0.04	0.85 ± 0.06

Abbreviation: BMI, body mass index.

Measurements

Satiety tests (weeks 1, 7 and 25)

The subjects arrived at 0800 hours in a fasted state at the laboratory. An intravenous catheter was inserted. After collection of the baseline blood sample ($t=0$ min), the subjects received either test or placebo yoghurt. For these test days, the same yoghurts were used as during the weight maintenance period. In total, 250 g yoghurt was provided as breakfast. The subjects were instructed to consume the yoghurt within 5 min. For the satiety tests, blood sampling was repeated after 90 and 180 min. The catheter was removed after the last blood sample had been taken. Ghrelin (Ghr), glucagon like peptide-1 (GLP-1) and cholecystokinin (CCK) were measured in the fasted state, and after 90 and 180 min to determine short-term satiety effects.

As part of the satiety tests, hunger was recorded hourly by Visual Analogue Scales (mmVAS) until 1300 hours.

The subjects were not allowed to eat during the morning and had only access to drinking water.

Blood parameters (weeks 1, 7 and 25)
During weeks 1, 7 and 25, a 46 ml blood sample was taken for hunger and satiety-related hormones (Ghr, GLP-1 and CCK) and FFA, TG, Gly and BHB. FFA, TG, Gly and BHB were measured in the fasted state only to determine the long-term effects. The hormones were determined in the fasted state as well as 90 and 180 min after yoghurt consumption as previously mentioned, to determine the long- as well as the short-term effects. The blood samples were mixed with ethylenediaminetetraacetate (EDTA) to prevent clotting. Samples for GLP-1 (4 ml) analysis were mixed with 40 μl of a dipeptidyl peptidase IV (DPP-IV) inhibitor (Linco Research Inc., St Charles, MO, USA) to prevent degradation. Samples for CCK analysis (4 ml) were mixed with 2000 KIU trasylol (Bayer Diagnostics Europe Ltd, The Netherlands). Plasma was obtained by centrifugation (4°C, 3000 r.p.m., 10 min), frozen in liquid nitrogen and stored at −20°C until further analysis. Plasma Ghr samples were mixed with HCl, methanol and phenylmethanesulfonyl fluoride (PMSF, Sigma-Aldrich, The Netherlands).

TG was measured using the GPO-trinder kit (Sigma Diagnostics Inc., St Louis, MO, USA), FFA were determined with the Wako NEFA C-kit (Wako Chemicals, Neuss, Germany), Gly with the glycerolkinase method (Boehringer Mannheim GmBH, Mannheim, Germany) and BHB with the β-hydroxybutyrate dehydrogenase method (Sigma Diagnostics Inc., St Louis, MO, USA). Plasma concentrations of active Ghr were measured by RIA (Linco Research Inc., St Charles, MO, USA).

Plasma active GLP-1 samples were analyzed using enzyme-linked immunosorbent assay (ELISA) (EGLP-35K; Linco Research Inc., St Charles, MO, USA). CCK was determined using RIA (Euria-CCK, Euro-Diagnostica AB, Malmö, Sweden).

Questionnaires (weeks 1, 7 and 25)
Attitude towards eating was analyzed in weeks 1, 7 and 25 in the fasted state using a validated Dutch translation of the Three Factor Eating Questionnaire (TFEQ).[9] Cognitive restrained and unrestrained eating behavior (F1), emotional eating and disinhibition (F2) and subjective feeling of hunger (F3) were scored 0 and 1 and summed. Higher scores denote higher levels of restrained eating, disinhibited eating and predisposition to hunger, respectively. In addition, as previously mentioned, during the satiety tests, hunger ratings were scored in the fasted state and every hour after yoghurt consumption until 1300 hours, as the subjective measurement represents in a robust and reproducible way the condition of the subject in this respect.[10] Subjects rated their hunger on visual analogue scales (VAS; in mm) by the pen and paper method. Hunger was rated on a 100 mm line preceded by the question 'How hungry do you feel?' and anchored on the left by 'not at all hungry' and on the right by 'as hungry as I have ever felt'. Subjects were instructed to make a single vertical mark at the appropriate point between the two anchors on each scale to indicate their subjective feeling of hunger at defined time points.

Changes in mood and tolerance of the treatment were determined in weeks 1, 7 and 25 in the fasted state. Mood (relaxed, gloomy, pleasant, angry, afraid, sad) was assessed with 100 mm VAS, and tolerance was determined using a questionnaire on the occurrence of complaints (headache, fatigue, nausea, stomachache, constipation, diarrhea, etc.) and scored. Frequency classification was: 0, never; 1, seldom; 2, sometimes; 3, relatively often; 4, often (five-point scale).

Anthropometry (weeks 2, 8 and 26)
Anthropometric measurements were taken in the fasted state during screening and in weeks 2, 8 and 26. Body weight was measured using a digital balance accurate to 0.02 kg (Chyo-MW-150 K, Chyo, Japan) with subjects in underwear after voiding their bladder. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (only during screening). The ratio of waist/hip circumference is an estimate of the distribution of body fat. The waist/hip ratio was calculated by dividing the waist circumference by the hip circumference. The waist circumference was measured at the site of the smallest circumference between the rib cage and the iliac crest, and the hip circumference was measured at the site of the largest circumference between the waist and the thighs. Both measurements were performed with subjects in standing position.

Body composition was measured in weeks 2, 8 and 26 using the ^2H_2O dilution technique.[11–13] The dilution of the ^2H isotope is a measure for total body water.[12] In the evening, the subjects ingested a dose of ^2H-enriched water (^2H_2O) after collecting a background urine sample. After ingestion of the ^2H solution, no further fluid or food consumption was permitted. The following morning, the second urine sample (second voiding) was collected. Deuterium concentration in the urine samples was measured using an isotope ratio mass spectrometer (Micromass Optima, Manchester, UK). Total body water was obtained by dividing the measured ^2H dilution space by 1.04 to correct for exchange of the ^2H label with nonaqueous hydrogen of body solids.[11] Fat-free mass (FFM) was calculated by dividing the total body water by hydrating factor 0.73. By subtracting FFM from body weight, fat mass (FM) was obtained. FM expressed as a percentage of body weight gives percentage of body fat. The analytic precision for ^2H is 0.2 ppm.[14]

Open-circuit, ventilated-hood test (weeks 2, 8 and 26)
In weeks 2, 8 and 26, the following EE and substrate oxidation variables were measured: REE, fat and carbohydrate oxidation for 30 min. The subjects were requested to arrive in the morning at the laboratory in the fasted state. REE and substrate oxidation were measured by means of an open-circuit ventilated-hood system with subjects lying supine for 30 min.[15] Gas analysis was performed by a

paramagnetic oxygen analyzer (omnical type 1155B, Crowborough Sussex, UK) and an infrared carbon dioxide analyzer (omnical type 1520/1507). EE was calculated using Weir's formula.[16] The respiratory quotient (RQ) was calculated as CO_2 produced/O_2consumed.

Statistical analysis

Data are presented as means and standard deviations. Data were analyzed using Statview s.e. + Graphics (Abacus Concepts, Berkeley, CA, USA, 1988). Differences over time and between the treatments (test or placebo yoghurt) over time were determined using one- and two-factor ANOVA with repeated measures. Differences between groups were analyzed using factorial ANOVA. Univariate linear regression was used to determine the relationship between selected variables. The level for establishing significant differences was taken at $P<0.05$.

Results

Characteristics of the subjects at baseline and after 6 weeks of weight loss are shown in Table 2 (anthropometric, eating behavior, tolerance, plasma lipids) and Table 3 (satiety related hormones). As presented in Table 2, there was a significant reduction in body weight during the VLED in both groups ($P<0.05$). The test and placebo group lost 7.76 ± 1.5 and 7.65 ± 1.4 kg, respectively. Apart from the decreased body weight, there were also reductions ($P<0.05$) in BMI, waist and hip circumference, FFM (kg), FM (kg and %), REE and RQ in both groups. FFM (%) was significantly increased in both groups after weight loss. The F1 score increased and the F2 score of the TFEQ decreased significantly in both groups ($P<0.05$). The F3 score was significantly decreased in the placebo group after weight loss ($P<0.05$). FFA were significantly increased after 6 weeks weight loss ($P<0.05$). Fasted blood values of BHB and TG, respectively, increased and decreased in both groups significantly ($P<0.05$). As presented in Table 3, there was, respectively, a significant decrease and increase in Ghrelin values at time point 0 and 180 during the weight loss period in the placebo group.

Figure 1 and Table 2 show the changes in body weight during the 18 weeks weight maintenance following weight loss. Surprisingly, there was no significant increase in body weight in the test group (1.13 ± 3.4 kg), whereas the placebo group showed a significant increase in body weight of 2.95 ± 3.1 kg (Figure 1, $P<0.001$). A difference in weight regain was shown between both groups (Figure 1, $P=0.05$ analysis of variance (ANOVA) two-factor repeated measures). Regain as % of weight loss was lower with test (15%) as compared to placebo yoghurt (40%) ($P=0.055$ factorial ANOVA).

As presented in Table 2, BMI and waist circumference did not increase in the test group, but significantly increased in the placebo group ($P<0.05$) during the weight maintenance period. For waist circumference, a treatment over time effect was seen during weight maintenance ($P<0.05$). FFM (kg) significantly increased in both groups during weight main-

Table 2 Subject characteristics before and after weight loss and after weight maintenance

	Week 1/2: before weight loss		*Week 7/8: after weight loss*		*Week 25/26: after weight maintenance*	
	Test group (n = 22)	*Placebo group (n = 28)*	*Test group (n = 22)*	*Placebo group (n = 28)*	*Test group (n = 22)*	*Placebo group (n = 28)*
Weight (kg)	81.3±8.6	79.0±8.6	73.5±8.6[a]	71.3±8.3[a]	74.7±8.3	74.3±9.0[b]
BMI (kg/m^2)	28.9±1.7	28.5±2.2	26.1±1.5[a]	25.8±2.2[a]	26.5±1.9	26.9±2.6[b]
Waist (cm)	91.1±5.6	91.5±7.7	83.9±5.9[a]	83.8±6.9[a]	83.6±5.0[c]	85.5±7.0[b]
Hip (cm)	108.8±4.3	108.1±7.1	103.0±5.5[a]	102.1±6.8[a]	102.1±7.3	102.9±8.5
FFM (kg)	50.0±5.9	48.3±4.5	48.3±6.4[a]	46.1±4.1[a]	49.9±6.0[b]	48.1±4.6[b]
FFM (%)	61.6±3.9	61.8±4.7	65.8±4.6[a]	65.0±5.6[a]	66.9±4.7[d]	65.2±6.1
FM (kg)	31.3±5.0	30.2±6.2	25.2±4.8[a]	25.3±6.3[a]	24.8±5.0[d]	26.1±7.0
FM (%)	38.4±3.9	38.2±4.7	34.2±4.6[a]	35.0±5.6[d]	33.1±4.7[d]	34.8±6.1
REE (MJ/day)[e]	6.3±0.8	6.5±0.7	6.0±0.7[a]	5.9±0.6[a]	6.5±0.8[b]	6.5±0.7[b]
RQ	0.83±0.05	0.82±0.04	0.79±0.04[a]	0.80±0.03[a]	0.86±0.05[b]	0.84±0.05[b]
F1 (TFEQ)	8.5±4.3	7.9±3.6	10.9±3.8[a]	11.6±4.4[a]	11.6±4.3	11.5±3.7
F2 (TFEQ)	7.2±2.7	7.0±2.1	6.1±2.8[a]	5.7±2.3[a]	6.1±2.6	6.0±2.1
F3 (TFEQ)	4.6±3.0	5.4±2.8	3.9±3.7	3.6±2.8[a]	4.1±3.7	3.3±2.7
Tolerance	12.7±6.9	11.3±8.3	13.6±7.9	12.3±9.0	12.0±6.5	10.8±7.4
FFA (μmol/l)	437.3±178.7	514.1±159.0	677.4±246.4[a]	635.3±168.[a]	348.1±116.1[b]	439.1±125.7[b]
BHB (μmol/l)	246.7±135.0	281.5±122.4	573.0±525.3[a]	417.1±211.0[a]	275.0±73.0[b]	303.3±111.4[b]
TG (μmol/l)	916.8±500.0	1003.1±599	636.1±263.3[a]	774.4±414.5[a]	792.9±327.2[b]	947.8±508.3[b]
glycerol (μmol/l)	97.3±44.7	110.1±41.8	110.6±43.8	107.7±35.8	109.0±53.4	115.3±40.1

Values are means±s.d. [a]$P<0.05$ over time difference compared to week 1/2 (ANOVA repeated measures). [b]*$P<0.05$* over time difference compared to week 7/8 (ANOVA repeated measures). [c]*$P<0.05$* treatment over time difference compared to week 7/8 (ANOVA repeated measures). [d]$P<0.05$ treatment over time difference compared to week 1/2 (ANOVA repeated measures). [e]Not corrected for FFM. For correction and statistical analysis, see Figure 2. Abbreviations: BHB, β-hydroxybutyrate; BMI, body mass index; factors 1, 2 and 3 of the TFEQ, Three Factor Eating Questionnaire: F1 = dietary restraint, F2 = disinhibition, F3 = general hunger; FFA, free fatty acids; FFM, fat-free mass; FM, fat mass; REE, resting energy expenditure; RQ, respiratory quotient; TG, triglycerides.

Table 3 Satiety-related hormones GLP-1, CCK and Ghr: values before and after weight loss and after weight maintenance

	Week 1/2: before weight loss		*Week 7/8: after weight loss*		*Week 25/26: after weight maintenance*	
	Test group (n = *22*)	*Placebo group* (n = *28*)	*Test group* (n = *22*)	*Placebo group* (n = *28*)	*Test group* (n = *22*)	*Placebo group* (n = *28*)
GLP-1 (pmol/l)						
*t*0 (fasted)	6.8±3.6	6.2±6.9	7.5±5.4	6.6±5.9	7.0±6.7	6.3±7.1
*t*90	7.9±6.5	6.7±5.9	7.8±5.1	7.6±6.5	7.5±6.8	7.3±7.8
*t*180	7.3±5.8	7.8±7.6	7.4±5.7	7.2±5.7	8.7±6.1[a]	7.5±8.1
CCK (pmol/l)						
*t*0 (fasted)	0.28±0.35	0.38±0.56	0.15±0.39	0.22±0.41	0.37±0.50[b]	0.48±0.89
*t*90	1.57±1.12	1.74±1.12	1.55±0.65	1.99±1.25	1.73±0.93	2.34±1.30
*t*180	0.40±0.56	0.72±0.84	0.33±0.48	0.42±0.56	0.17±0.22	0.58±0.92
Ghr (pg/ml)						
*t*0 (fasted)	120.7±63.9	124.8±49.5	101.4±57.9	105.4±53.2[c]	162.5±130.1[b]	128.1±41.5[b]
*t*90	62.1±34.0	63.5±33.3	64.3±37.1	83.3±81.7	124.2±111.0[b]	91.2±28.9
*t*180	142.9±68.6	128.7±60.4	163.9±61.7	168.9±89.9[c]	132.2±81.3	122.7±54.5[b]

Values are means±s.d. [a]$P<0.05$ treatment over time compared to week 1/2 (ANOVA repeated measures). [b]$P<0.05$ over time difference compared to week 7/8 (ANOVA repeated measures). [c]$P<0.05$ over time difference compared to week 1/2 (ANOVA repeated measures). Abbreviations: ANOVA, analysis of variance; CCK, cholecystokinin; Ghr, ghrelin active; glp-1, glucagon-like peptide 1.

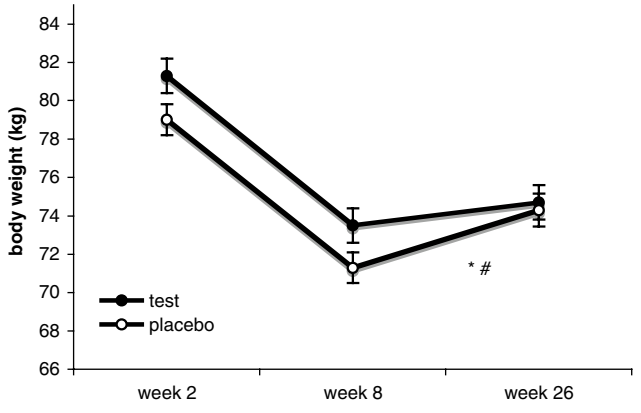

Figure 1 Changes in body weight (kg). Values are means±s.e.m. *$P<0.001$ regain (kg) in placebo group (over time effect, ANOVA repeated measures). #$P=0.05$ treatment over time (ANOVA repeated measures).

tenance. As an overall effect, a treatment over time effect (week 26 compared to week 2) was seen for FFM (%) and FM ($P<0.05$), in that the test group increased in FFM (%) and decreased in FM compared to placebo. RQ was significantly increased during the weight maintenance period, in both groups ($P<0.05$). Fasted values of FFA and BHB decreased in both groups, and TG increased in both groups during weight maintenance ($P<0.05$). Hip circumference, F1, F2 and F3 (TFEQ), tolerance and glycerol showed no significant over time differences. Concerning mood values, no significant differences between groups were seen (data not shown).

There was a significant linear relation between REE (MJ/day) and FFM (kg) in week 2 and 26 in both groups, $P<0.05$, Figure 2a and b. To determine for each group whether changes in REE took place over time as a function of FFM (REE regressed against FFM), FFM of week 26 was filled in the regression equation of week 2 to calculate the 'predicted' REE (MJ/day). ANOVA repeated measures showed that the measured REE in week 26 was significantly higher ($P<0.05$) than the predicted REE in week 26 for the test group, but not for the placebo group (Figure 2c). A comparison of the two groups with regard to differences between the predicted and measured REE in week 26 did not reach a significantly different treatment over time effect.

Table 3 presents the GLP-1, CCK and Ghr values at baseline and before and after weight maintenance. GLP-1 values at 180 min after yoghurt consumption were significantly increased at week 25 compared to week 1 in the test group, but not in the placebo group (treatment over time effect, $P<0.05$). During weight maintenance, CCK in the fasted state was significantly increased in the test group ($P<0.05$). Ghr was significantly increased in both groups in the fasted state, was significantly increased in the test group at 90 min after yoghurt consumption and was significantly decreased in the placebo group at 180 min after yoghurt consumption ($P<0.05$).

Hunger ratings (average hunger from 0900 to 1300 hours) at baseline and before and after weight maintenance are presented in Table 4 and Figure 3. A significant difference was found between the test and placebo group in week 25, in that the test group was less hungry 4 h after yoghurt consumption (Table 4, $P<0.05$ factorial ANOVA).

Discussion

The present study shows that daily consumption of 500 g Olibra yoghurt (with 10 g Olibra® emulsion) during approximately 4 months supported moderate overweight subjects in maintaining their loss in body weight without inducing macronutrient imbalance.

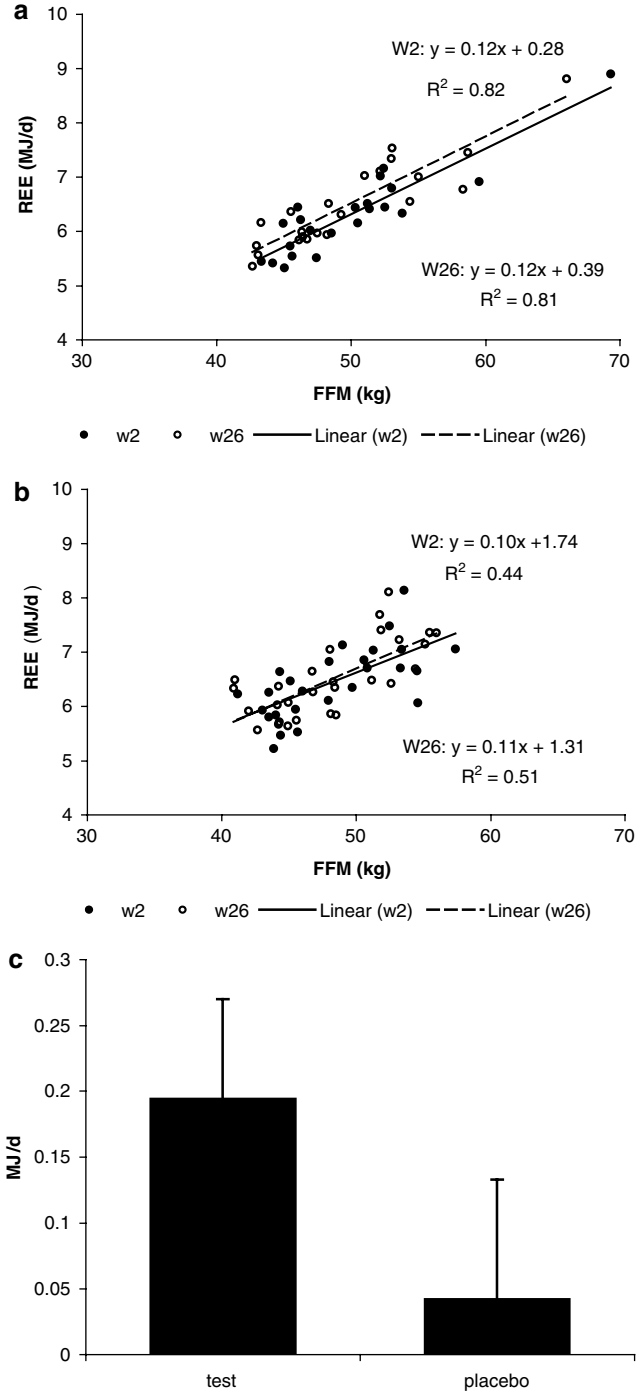

Figure 2 (**a**) REE (MJ/day) as a function of FFM (kg) plotted for week 2 and week 26 in the test group. (**b**) REE (MJ/day) as a function of FFM (kg) plotted for week 2 and week 26 in the placebo group. (**c**) Week 26: measured REE minus predicted REE. Values are means ± s.e.m.

The better weight maintenance upon consumption of test (Olibra) yoghurt compared to placebo (1.2 vs 3.0 kg regain), as well as the sustained reduced waist circumference, is explained by the relatively lower increase in hunger paralleled by a higher increase in GLP-1 during weight maintenance and by the relatively higher REE as a function of FFM.

As FFM is the main determinant of REE, REE should be corrected for FFM.[17] We corrected REE for FFM by expressing REE as a function of FFM. The present study shows that REE as a function of FFM did increase significantly (measured REE vs predicted REE) in the test group during the study period, whereas no significant increase in the placebo group was seen. As our data were analyzed with REE corrected for FFM, the increase in REE in the test group could not be explained by changes in FFM and therefore is attributed to the Olibra yoghurt. More research, however, is needed to elucidate the mechanism.

Our interpretation is that when weight maintenance starts, it is supported when at the same time a so-called fat-free mass sparing effect occurs. Previously, Dulloo *et al*.[18] described this sparing effect in which the body composition of a given individual changes continuously towards a leaner body composition during the course of starvation. In our study, we found that FM is more decreased in the test group compared to the placebo group during the whole study period, which implies a higher percentage FFM in the test group. This FFM sparing effect stimulates REE and thus prevents a decreased REE. A decreased REE is responsible for the weight cycling effect. A reduction in REE usually causes weight regain as, during weight maintenance, subjects start eating again as usual while the energy requirement has been reduced.[19] Accordingly, fat oxidation is sustained. These factors seem to be the condition for weight maintenance, as we showed before.[20–23]

During weight maintenance, the waist circumference is decreased (−0.3 cm) in the test group, while it is increased (+1.7 cm) in the placebo group ($P<0.05$). Visscher *et al*.[24] concluded that waist circumference is a better indicator of changes in energy balance and energy-balance-related behavior than BMI. This finding supports the beneficial effects of the test yoghurt. Furthermore, waist circumference reflects abdominal or intra-abdominal fat and this fat has been associated with adverse clinical effects, characterized by hyperinsulinemia, dyslipidemia, glucose intolerance, diabetes, cardiovascular diseases and some cancers.[25] Therefore, waist circumference for given levels of BMI can be used to predict health risks associated with overweight and obesity.[26]

No effect of the test yoghurt on fat oxidation or fat-related blood parameters (FFA, BHB, TG and Gly) was seen. Furthermore, mood and tolerance were not affected by test yoghurt consumption. The changes in dietary restraint (F1), emotional eating (F2) and the general feeling of hunger (F3) did not differ between the groups and cannot explain the better weight maintenance with test yoghurt.

A group of Irish researchers conducted three short-term human studies with a double-blind, placebo-controlled, within-subject crossover design in which participants were offered 200 g portions of either placebo or Olibra yoghurt (with either 5, 10, 12.5 or 15 g emulsion equaling 2, 4, 5 or

Figure 3 Hunger scores in week 1, 7 and 25. Values are means. 0900 hours: hunger score before yoghurt consumption. 1000 hours: hunger score 1 h after yoghurt consumption. 1300 hours: hunger score 4 h after yoghurt consumption.

Table 4 Hunger scores at baseline (week 1) and before (week 7) and after (week 25) weight maintenance

	Average hunger from 0900–1300 hours	
	Test group (n = *22*)	*Placebo group* (n = *28*)
Week 1/2	29.4 ± 24.9	34.5 ± 33.2
Week 7/8	26.1 ± 24.5	30.3 ± 22.3
Week 25/26	29.4 ± 21.8	45.6 ± 30.0[a]

Values are means ± sd. 0900 hours: hunger score before yoghurt consumption. 1000 hours: hunger score 1 h after yoghurt consumption. 1300 hours: hunger score 4 h after yoghurt consumption. [a]$P < 0.05$ test group compared to placebo group, factorial ANOVA. Abbreviation: ANOVA, analysis of variance.

6 g Olibra fat, respectively). They investigated the hunger feelings after consumption of Olibra yoghurt. Despite reduced subsequent energy intake, contradictory results were seen in hunger and satiety recordings.[5–7] A study by Logan *et al*.[27] failed to confirm the short-term reduction in food intake. Furthermore, the Olibra emulsion did not appear to exert any suppressive effects on appetite ratings in the medium-term (up to 3 weeks). In the present study, hunger scores during 4 h after morning consumption of test yoghurt were decreased at the end of the weight maintenance period, but not at baseline or after weight loss. Food intake was not evaluated in this study.

The mechanism of action of the novel fat emulsion is not precisely understood. It is thought that the satiating power of the Olibra emulsion is owing to the physio-chemical stability of the emulsion, rather than the constituent of the emulsion *per se*.[27] The observed effects of the novel fat emulsion have been suggested to be the result of the 'ileal brake' mechanism.[5–7] This ileal brake, for which fat is the most important trigger, initiates a feedback loop that inhibits upper gut motility (to slow gastric emptying and intestinal transit) in response to nutrients in the distal small intestine.[28–30] The palm oil core of the relatively small emulsion particles is covered by hydrophilic galactolipids derived from the fractionated oat oil. Owing to this particular combination of triglyceride oils, resulting in delayed digestion compared to the milk fat particles, (partly) undigested particles may penetrate more distal parts of the small intestine, where sensors will detect unabsorbed fat and send satiety signals to the brain. As the ileal brake mechanism appears to be related to the release of one or more satiety hormones from the distal intestine,[29,31,32] Ghr, GLP-1 and CCK were determined in this study. Indeed, in the long-term, GLP-1 values at 180 min after test yoghurt consumption in week 25 were significantly increased compared to baseline levels. Thus our findings may support the ileal brake theory indirectly as an explanation for the Olibra effects in the longer term. The increased GLP-1 values after weight maintenance are in line with the reduced hunger feelings after consumption of test yoghurt at that time point.

Taken together, our results show that the previously observed short-term effects of Olibra-containing yoghurts on energy intake and hunger/satiety scores are not counteracted by compensation behavior during long-term use. Furthermore, long-term use has beneficial effects on body composition and weight maintenance.

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Disclosure of conflict of interest

The study was sponsored by Campina Innovation, Wageningen, The Netherlands, which raises potential duality of interest.

References

1 Seidell JC. Dietary fat and obesity: an epidemiologic perspective. *Am J Clin Nutr* 1998; **67**: 546S–550S.
2 Stunkard AJ. Current views on obesity. *Am J Med* 1996; **100**: 230–236.
3 Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992; **16**: 397–415.
4 Van Gaal LF, Wauters MA, De Leeuw IH. The beneficial effects of modest weight loss on cardiovascular risk factors. *Int J Obes Relat Metab Disord* 1997; **21** (Suppl 1): S5–S9.
5 Burns AA, Livingstone MB, Welch RW, Dunne A, Reid CA, Rowland IR. The effects of yoghurt containing a novel fat emulsion on energy and macronutrient intakes in non-overweight, overweight and obese subjects. *Int J Obes Relat Metab Disord* 2001; **25**: 1487–1496.
6 Burns AA, Livingstone MB, Welch RW, Dunne A, Robson PJ, Lindmark L *et al*. Short-term effects of yoghurt containing a novel fat emulsion on energy and macronutrient intakes in non-obese subjects. *Int J Obes Relat Metab Disord* 2000; **24**: 1419–1425.
7 Burns AA, Livingstone MB, Welch RW, Dunne A, Rowland IR. Dose–response effects of a novel fat emulsion (Olibra) on energy and macronutrient intakes up to 36 h post-consumption. *Eur J Clin Nutr* 2002; **56**: 368–377.
8 Harris JA, Benedict FG. *A Biometric Study of Basal Metabolism in Man*. Carnegia Institution: Washington, 1919.
9 Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *J Psychosom Res* 1985; **29**: 71–83.
10 Raben A, Holst JJ, Christensen NJ, Astrup A. Determinants of postprandial appetite sensations: macronutrient intake and glucose metabolism. *Int J Obes Relat Metab Disord* 1995; **20**: 161–169.
11 Schoeller DA, van Santen E, Peterson DW, Dietz W, Jaspan J, Klein PD. Total body water measurement in humans with 18O and 2H labeled water. *Am J Clin Nutr* 1980; **33**: 2686–2693.
12 van Marken Lichtenbelt WD, Westerterp KR, Wouters L. Deuterium dilution as a method for determining total body water: effect of test protocol and sampling time. *Br J Nutr* 1994; **72**: 491–497.
13 Westerterp KR, Wouters L, van Marken Lichtenbelt WD. The Maastricht protocol for the measurement of body composition and energy expenditure with labeled water. *Obes Res* 1995; **3** (Suppl 1): 49–57.
14 Forsum E, Kabir N, Sadurskis A, Westerterp K. Total energy expenditure of healthy Swedish women during pregnancy and lactation. *Am J Clin Nutr* 1992; **56**: 334–342.
15 Adriaens MP, Schoffelen PF, Westerterp KR. Intra-individual variation of basal metabolic rate and the influence of daily habitual physical activity before testing. *Br J Nutr* 2003; **90**: 419–423.
16 Weir JBDV. New methods for calculating metabolic rate with special references to protein metabolism. *J Physiol* 1949; **109**: 1–9.
17 Ravussin E, Bogardus C. A brief overview of human energy metabolism and its relationship to essential obesity. *Am J Clin Nutr* 1992; **55**: 242S–245S.
18 Dulloo AG, Jacquet J. The control of partitioning between protein and fat during human starvation: its internal determinants and biological significance. *Br J Nutr* 1999; **82**: 339–356.
19 Kempen KP, Saris WH, Westerterp KR. Energy balance during an 8-wk energy-restricted diet with and without exercise in obese women. *Am J Clin Nutr* 1995; **62**: 722–729.
20 Adam TC, Westerterp-Plantenga MS. Nutrient-stimulated GLP-1 release in normal-weight men and women. *Horm Metab Res* 2005; **37**: 111–117.
21 Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. *Br J Nutr* 2005; **93**: 281–289.
22 Westerterp-Plantenga MS, Lejeune MP, Kovacs EM. Body weight loss and weight maintenance in relation to habitual caffeine intake and green tea supplementation. *Obes Res* 2005; **13**: 1195–1204.
23 Westerterp-Plantenga MS, Lejeune MP, Nijs I, van Ooijen M, Kovacs EM. High protein intake sustains weight maintenance after body weight loss in humans. *Int J Obes Relat Metab Disord* 2004; **28**: 57–64.
24 Visscher TL, Seidell JC. Time trends (1993–1997) and seasonal variation in body mass index and waist circumference in the Netherlands. *Int J Obes Relat Metab Disord* 2004; **28**: 1309–1316.
25 Bigaard J, Tjonneland A, Thomsen BL, Overvad K, Heitmann BL, Sorensen TI. Waist circumference, BMI, smoking, and mortality in middle-aged men and women. *Obes Res* 2003; **11**: 895–903.
26 Bigaard J, Frederiksen K, Tjonneland A, Thomsen BL, Overvad K, Heitmann BL *et al*. Waist circumference and body composition in relation to all-cause mortality in middle-aged men and women. *Int J Obes (Lond)* 2005; **29**: 778–784.
27 Logan CM, McCaffrey TA, Wallace JM, Robson PJ, Welch RW, Dunne A *et al*. Investigation of the medium-term effects of Olibratrade mark fat emulsion on food intake in non-obese subjects. *Eur J Clin Nutr* 2006; **60**: 1081–1091.
28 Spiller RC, Trotman IF, Higgins BE, Ghatei MA, Grimble GK, Lee YC *et al*. The ileal brake – inhibition of jejunal motility after ileal fat perfusion in man. *Gut* 1984; **25**: 365–374.
29 Van Citters GW, Lin HC. The ileal brake: a fifteen-year progress report. *Curr Gastroenterol Rep* 1999; **1**: 404–409.
30 Symerski T, Kee B, Haddeman E, Peters H, Masclee A. Ileal brake effects on satiety and meal intake in humans after a meal replacer (abstract). *Int J Obes Relat Metab Disord* 2004; **28** (Suppl 1): S148.
31 Aponte GW, Fink AS, Meyer JH, Tatemoto K, Taylor IL. Regional distribution and release of peptide YY with fatty acids of different chain length. *Am J Physiol* 1985; **249**: G745–G750.
32 Jin H, Cai L, Lee K, Chang TM, Li P, Wagner D *et al*. A physiological role of peptide YY on exocrine pancreatic secretion in rats. *Gastroenterology* 1993; **105**: 208–215.