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The emulsified lipid Fabuless (Olibra) does not decrease food intake but suppresses appetite when consumed with yoghurt but not alone or with solid foods: A food effect study

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ABSTRACT

The lipid emulsion Fabuless (Olibra) has been shown in some studies to decrease short/medium term energy intake (EI) and prevent weight regain. The purported mechanism is the ileal brake. Whether Fabuless is efficacious under a range of dietary conditions is unknown since studies have administered the emulsion within a fermented, semi-liquid dairy yoghurt, and outcomes have been inconsistent. To determine whether Fabuless suppresses post-ingestive satiety and short-term food intake under a range of dietary conditions and forms we administered the emulsion co-presented with 185 mL water, stirred into a semi-liquid dairy yoghurt, and co-presented with a solid food breakfast muffin. This was a cross-over study in 18 lean men randomised to 6 treatments: (i) lipid emulsion, LE (15 g Fabuless, containing 4.2 g lipid, 0.2 MJ) + water, (ii) lipid control, LC (15 g non-emulsified lipid/water, containing 4.2 g lipid, 0.2 MJ) + water, (iii) lipid emulsion + yoghurt, LE + Y (1.2 MJ), (iv) lipid control + yoghurt, LC + Y (1.2 MJ), (v) lipid emulsion + muffin, LE + M (1.2 MJ), (vi) lipid control + muffin, LC + M (1.2 MJ), each given as a test breakfast at 8.30 am. Participants rated postprandial appetite sensations using visual analogue scales (VAS), and *ad libitum* energy intake was measured at a lunch meal 3.5 h later. The lipid emulsion increased fullness compared with an energy-matched lipid control but only when administered within the semi-liquid fermented yoghurt ($P<0.05$). There were no effects on satiety ratings when co-presented with water or with the solid food muffin. Energy and macronutrient intake were not significantly decreased by any of the emulsion treatments. We conclude that effects are small, the format in which lipid emulsions are consumed influences postprandial satiety, and there is no evidence that this emulsion alters eating behaviour at the subsequent meal.

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1. Introduction

Degree of emulsification and emulsion stability has long been known to be important characteristics of lipids [1–3], and studies have shown that lipid emulsions may enhance satiety [4–7].[1] 'Fabuless' (Olibra) is a lipid emulsion containing fractionated palm and oat oils dispersed in water which has been shown to decrease hunger and/or food intake, with effects lasting for up to 36 h[4,5] and following low lipid doses of 2 g, 4 g and 6 g [6], although these effects are not seen in all studies [8], in all study participants [9], or in all food sources or conditions [10]. Nevertheless, it has been shown to aid weight maintenance following periods of weight loss [7]. The proposed, although as yet largely unsupported, mechanism for emulsified lipids such as Fabuless is the ileal brake [11] where emulsified oils may delay lipolysis and fat absorption from the proximal duodenum [12], the usual site of small bowel absorption, to the distal ileum which is then exposed to an unusually high intraluminal fat content. This may stimulate a feedback loop which in turn slows gastric emptying, jejunal motility and may promote secretion of satiety-enhancing gastrointestinal peptides [13]. This is an idea supported by early studies of lipid infusion into the distal ileum [1,14,15] which has recently been reconfirmed in tube feeding studies showing that even very small amounts of fat (3 g) entering the ileum may alter satiety ratings of hunger and fullness [16].

In light of recent renewed interest in the anorectic effects of lipid emulsions [10,11], it is important to note several things. Firstly, not all investigations of Fabuless have been able to show enhanced postprandial satiety and/or a change in eating behaviour [8–10]; secondly, this emulsion has been tested only under very limited dietary conditions, specifically within a fermented, semi-liquid, dairy yoghurt;

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[1] 'Fabuless' and 'Olibra' are trademarks.

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and thirdly, supportive evidence for the ileal brake mechanism remains elusive following oral intake of lipids with only one study providing evidence of a longer oro-caecal transit time [17].

Since published studies to date have administered the emulsion within semi-liquid dairy yoghurt, we were particularly interested in assessing the postprandial effects of emulsions across a range of dietary conditions. It is likely that the presence of other foods may alter the passage of the emulsion through the gastrointestinal (GI) tract. For example, both energy [18] and macronutrient [19] content of a meal are determinants of factors such as rate of gastric emptying, as may be physical form [20], and common food processing techniques [10]. These may in turn affect satiety related signaling and hunger suppression.

To determine whether the emulsion Fabuless could suppress postingestive satiety and short-term food intake across different dietary conditions we gave a 15 g lipid and water emulsion (Fabuless, containing 4 g lipid) to a group of male participants at breakfast: (i) with 185 mL water, (iii) stirred into a semi-liquid fermented dairy yoghurt and (iii) co-presented with a solid food savoury muffin, and assessed appetitive sensations and energy intake from a subsequent *ad libitum* lunch meal.

2. Participants and methods

2.1. Participants

Male participants who were lean (body mass index, BMI 18–25 kg/m^2), aged between 18 and 55 years and healthy by self-report were registered into this intervention trial. Recruitment was carried out in the wider Auckland area through poster, newspaper and electronic advertisement. Participants came fasted to the appetite research centre at the Auckland Human Nutrition Unit (HNU) as previously described [21,22] for screening, at which time anthropometric measurements comprising body weight, height, waist circumference and blood pressure were measured. Exclusion criteria included self-reported history of overweight or obesity or eating disorders, current dieter or cigarette smoker, as well as hypertension, cardiovascular disease, diabetes mellitus (type I or II), and any other significant metabolic, endocrine or gastrointestinal disease. None of the participants were taking medications known to affect appetite or weight regulation. Ethical approval for this study was obtained from the Northern Region X, Health and Disabilities Ethics Committee, Auckland, New Zealand and written consent to participate was obtained from each of the study volunteers. This study is registered with the Australia New Zealand Clinical Trials Registry (No. 12609000851268).

2.2. Study design

In this study the short-term effects of the commercial lipid emulsion Fabuless and an energy and fatty acid matched control lipid given with either (i) water, (ii) a semi-liquid or (iii) a solid food item, were assessed using visual analogue scales (VAS) and direct quantitative measurement of energy intake (EI) at a restricted buffet lunch meal. All participants attended the HNU on 6 separate occasions where they were randomly allocated to one of six study treatments. Between each visit they returned home for a minimum 2 day washout period where they were free to resume their usual diet and exercise patterns. Participants were asked to abstain from alcohol, significant changes in their habitual diet, and strenuous physical activity for 24 h prior to the study-day. In order to encourage compliance on the pre-treatment day participants were asked to record their 24 h dietary intake and physical activity level which was estimated as time spent standing, sitting, watching TV/computer activities, or engaged in mild-moderate and vigorous-strenuous activity.

2.3. Procedures

The single day protocol used in this study was based upon the recent consensus document of Blundell and colleagues [23]. On each study day participants were asked to fast from 8 pm the previous evening and avoid morning exercise. Upon arrival at the HNU, body weight was measured whilst lightly clad (Seca, Model 708, Germany) and any adverse events recorded. Height was measured on a single occasion at the screening visit (Seca, Model 222, Germany). Participants were given 200 mL of water to drink. The daily study protocol showing the timing of the breakfast and the *ad lib* lunch is shown in Fig. 1. At 0800 h baseline VAS rating feelings of hunger, fullness, satisfaction and current thoughts of food (TOF)/prospective consumption were completed [23]. The test breakfast, which contained either an emulsion or non-emulsion lipid, was served at 0830 h with 185 mL of water and participants were asked to consume the meal in full but at their own pace within 15 min. No further foods were allowed throughout the morning and the participants remained within the HNU until an *ad lib* lunch meal was served at 1200 h (210 min later). VAS ratings were measured throughout the morning and for 2 h after completion of the lunch. Lunch was served in individual dining rooms and no distractions were allowed during the 30 min lunch period. Participants remained at the HNU throughout each study day and were allowed to read, use laptop computers or undertake other similar sedentary activities but were not allowed to sleep.

2.4. Lipid treatments

The lipid plus water emulsion (LE) and the lipid plus water control (LC, non-emulsion) were isoenergetic (0.2 MJ) and closely matched for fatty acid (f.a.) composition (Fabuless: 42% C16:0; 40% C18:1; 10% C18:2; 8% other f.a.s; Palm olein control: 40% C16:0; 43% C18:1; 12% C18:2; 5% other f.a.s). The 15 g LE given to participants comprised 4.2 g lipid and 10.8 g water in a smooth emulsion. The matched 15 g

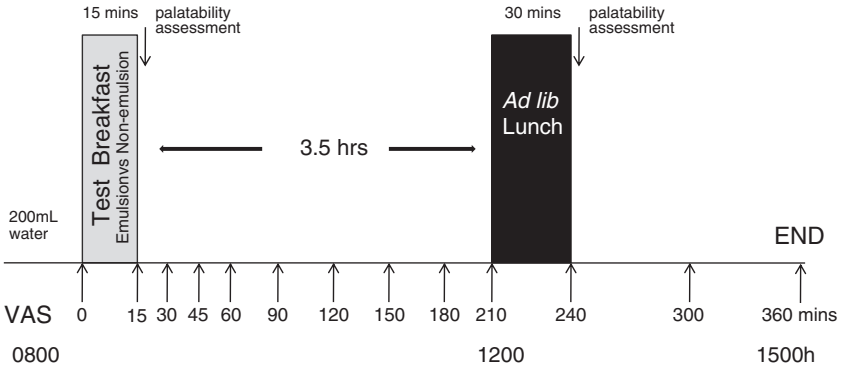

Fig. 1. Daily protocol for the study.

non-emulsified LC also comprised 4.2 g lipid and 10.8 g water which remained unmixed with each presented to the participants individually on a spoon. In the first pair of treatments (LE, LC) the lipids were consumed alone at breakfast with only a 185 mL glass of tap water. In the second pair of treatments the lipids described above were stirred into a semi-liquid yoghurt immediately before the breakfast was served (LE + Y, LC + Y). In the third pair of treatments the lipids were co-presented with a solid food breakfast muffin and an 81 mL glass of tap water (LE + M, LC + M). The total weight of each breakfast was 200 g. Hence the 6 treatments were (i) 15 g lipid/water emulsion, LE (Fabuless, containing 4.2 g lipid,0.2 MJ) + 185 mL water, (ii) 15 g lipid/water control, LC (non-emulsified, containing 4.2 g lipid, 0.2 MJ) + 185 mL water, (iii) 15 g lipid emulsion + yoghurt, LE + Y (1.2 MJ), (iv) 15 g lipid control + yoghurt, LC + Y (1.2 MJ), (v) 15 g lipid emulsion + muffin, LE + M (1.2 MJ), (vi) 15 g lipid control + muffin, LC + M (1.2 MJ). The f.a. composition of the commercial lipid emulsion and control lipids was matched as closely as possible. The commercial emulsion was purchased from a retail outlet in New Zealand. In order to standardize the energy density (ED; 6.0 kJ/g) of the semi-liquid yoghurt and solid food muffin treatments, 81 mL of water was given at breakfast with the muffin. The energy and macronutrient composition of the 6 test breakfasts was calculated using the dietary program FoodWorks™ (Professional Edition, Version 5, 1998–2007; Xyris Software, Australia) and are shown in Table 1.

2.5. Visual analogue scales (VAS)

Participants rated their hunger, fullness, satisfaction and TOF using VAS. The questions asked were "How hungry do you feel?", "How full do you feel?", "How satisfied do you feel?" and "How much do you think you can eat now?". Subjective feelings were recorded on paper by placing a vertical line across 100 mm scales, anchored at either end by statements; "I am not hungry at all/I am not full at all/I am completely empty/ nothing at all" on the left and "I am as hungry as I have ever been/I am totally full/I cannot eat another bite/a large amount" on the right. VAS rating nausea and how thirsty, energetic and relaxed the participants felt were also completed. VAS were completed prior to the test breakfast (0 min, baseline), and then at 15 (end of test breakfast), 30, 45, 60, 90, 120, 150, 180, 210 (*ad lib* lunch), 270, 330 and 360 min. Immediately after breakfast, participants also rated the pleasantness, visual appeal, smell, taste, aftertaste and overall palatability of the breakfast on separate 100-mm VAS. These questions were anchored on the left by the statements "not at all pleasant (pleasantness)/bad (visual appeal, smell, taste, palatability)/none (aftertaste)" and on the right by the statements "as pleasant as I have ever tasted (pleasantness)/good (visual appeal, smell, taste, palatability)/much (aftertaste)".

2.6. Ad libitum lunch

The *ad lib* lunch consisted of a restricted buffet-style meal. In an attempt to avoid over-consumption the variation of meal items offered was limited. Participants were advised that they could eat as much or as little as they chose, to eat until they were comfortably full and asked to remain in their individual room for a period of 30 min. When they had finished eating they raised an 'I am full' sign. The items presented at the *ad lib* buffet meal, along with the portion sizes, energy and macronutrient content are shown in the lower half of Table 1. All discrete items (ham sandwiches, carrot and raisin loaf, tinned peaches) were presented as small bite size portions, and all items were served in moderate excess with the intent that participants would not consume the entirety of any single item. Each meal item was weighed before and after the lunch meal to the nearest 0.5 g (Sartorius AG, Goettingen, Germany), and the energy and macronutrient content of the foods calculated using the dietary program FoodWorks.

2.7. Statistical analysis

VAS data assessing the palatability of the 6 breakfast meals and the energy and macronutrient intake data from the *ad lib* lunch was analysed using repeated measures Linear Mixed Model ANOVA (SAS: PROC MIXED, SAS version 9.2, SAS Institute Inc, Cary, NC, USA, 243 2002–2008). VAS data assessing postprandial feelings of hunger, fullness and other appetite-related sensations throughout each study visit were also analysed using repeated measures Linear Mixed Model ANOVA where the participant, dietary preload, study period and study day were included in the procedure, in addition to the treatment/time interaction which addressed whether the trajectory over time during the study period differed between the breakfast treatments (diet × time). Where the ANOVA was significant, Tukey's post hoc analysis was used for comparisons between treatments. Time to

Table 1
Energy and macronutrient composition of the six test-breakfast preloads and the *ad libitum* lunch items.

	Emulsion lipid/water (g)	Control lipid/water (g)	Yogurt^/ muffin+ (g)	Water to drink (g)	Total weight (g)	Energy (kJ)	ED (kJ/g)	Fat (g)	Fat (%en)	CHO (g)	CHO (%en)	Protein (g)	Protein (%en)
Breakfast preloads													
LE*	15	0	-	185	200	155	0.8	4.2	100	0	0	0	0
LC*	0	15	-	185	200	156	0.8	4.2	100	0	0	0	0
LE + yoghurt^	15	0	185^	0	200	1200	6	15.9	50	29	38	7	10
LC + yoghurt^	0	15	185^	0	200	1200	6	15.9	50	29	38	7	10
LE + muffin+	15	0	103+	81	199	1172	5.9	15.5	50	27.8	37	6.8	10
LC + muffin+	0	15	103+	81	199	1172	5.9	15.5	50	27.8	37	6.8	10
Lunch items													
Chicken fried rice	-	-	-	-	931	4636	5.0	30.3	25	166.3	56	39.3	14
Ham sandwiches, white bread, ¼ slices	-	-	-	-	580	5596	9.6	42	28	166.8	47	60.8	18
Carrot and raisin loaf, ¼ slices	-	-	-	-	200	2920	14.6	21.6	28	114	61	9.8	6
Peaches, tinned in fruit juice, slices, drained	-	-	-	-	820	1480	1.8	0.8	2	77.9	83	4.1	5
Bottled water, still	-	-	-	1500	1500	0	0	0	0	0	0	0	0

Lipid emulsion (LE; 4.2 g lipid + 10.8 g water, emulsified; Fabuless comprising a high-saturated fatty acid (SFA) fractionated palm oil triglyceride with an oat oil galactolipid emulsifying coat: 42% C16:0; 40% C18:1; 10% C18:2; 8% other fatty acids) and matched non-emulsified lipid control (LC; 4.2 g lipid + 10.8 g water, non-emulsified but consumed together; comprising high-SFA palm olein: 40% C16:0; 43% C18:1; 12% C18:2; 5% other fatty acids) were co-presented alone with a glass of water*, stirred into a semi-liquid yoghurt^, and co-presented with a solid food muffin+ and water. The total weight of each breakfast was 200 g. ED, energy density; CHO, carbohydrate; % en, percentage of energy

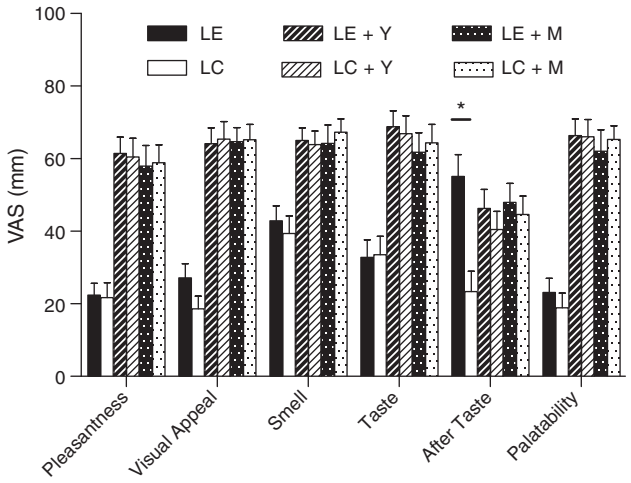

Fig. 2. Mean (sem) visual analogue scale (VAS) ratings for palatability for each of the 6 test breakfasts. Aftertaste was significantly worse for the lipid emulsion (LE) compared with the lipid control (LC) when served alone with water ($P<0.05$). No other significant differences were detected. LE + Yoghurt (LE + Y), LC + Yoghurt (LC + Y), LE + Muffin (LE + M), LC + Muffin (LC + M).

return to pretreatment baseline for VAS hunger, fullness, satisfaction and TOF was analysed using the Friedman nonparametric procedure (SPSS version 18.0.2, SPSS Inc, Chicago, Il, USA, 2010) in order to assess the possibility of preloads resulting in 'suppression of hunger for longer' and 'fuller for longer' across treatment conditions. Statistical significance was set at a level of 0.05.

3. Results

3.1. Participants

Eighteen healthy, male participants from the Auckland region were recruited into the study and completed the 6 preload days in randomised order. The participants had a mean age of 36 (16, sd) years, were lean with a mean BMI of 22 (2, sd) kg/m^2, and healthy by self-report. There were no differences in either reported EI ($P>0.05$) or reported level of physical activity (hours sitting, hours standing, moderate activity, vigorous activity; all, $P>0.05$) on the day prior to each of the study days when compared between treatment groups. This was in line with the request that participants did not schedule visits to the appetite research centre following significant dietary, social or sporting events.

3.2. Visual analogue scales

3.2.1. Palatability

As may be expected at the test breakfast, VAS-assessed pleasantness, visual appeal, smell, taste, and overall palatability were significantly higher when the emulsion and control lipids were combined with the dairy yoghurt (LE + Y, LC + Y) or co-presented with the breakfast muffin (LE + M, LC + M), than when they were given with water alone (LE, LC; $P<0.05$, see Fig. 2). However, when comparing between emulsion and control within each of the 3 food groups (water only: LE vs LC; yoghurt: LE + Y vs LC + Y; muffin: LE + M vs LC + M), there was little difference in post-breakfast ratings ($P>0.05$) other than for aftertaste which rated significantly worse

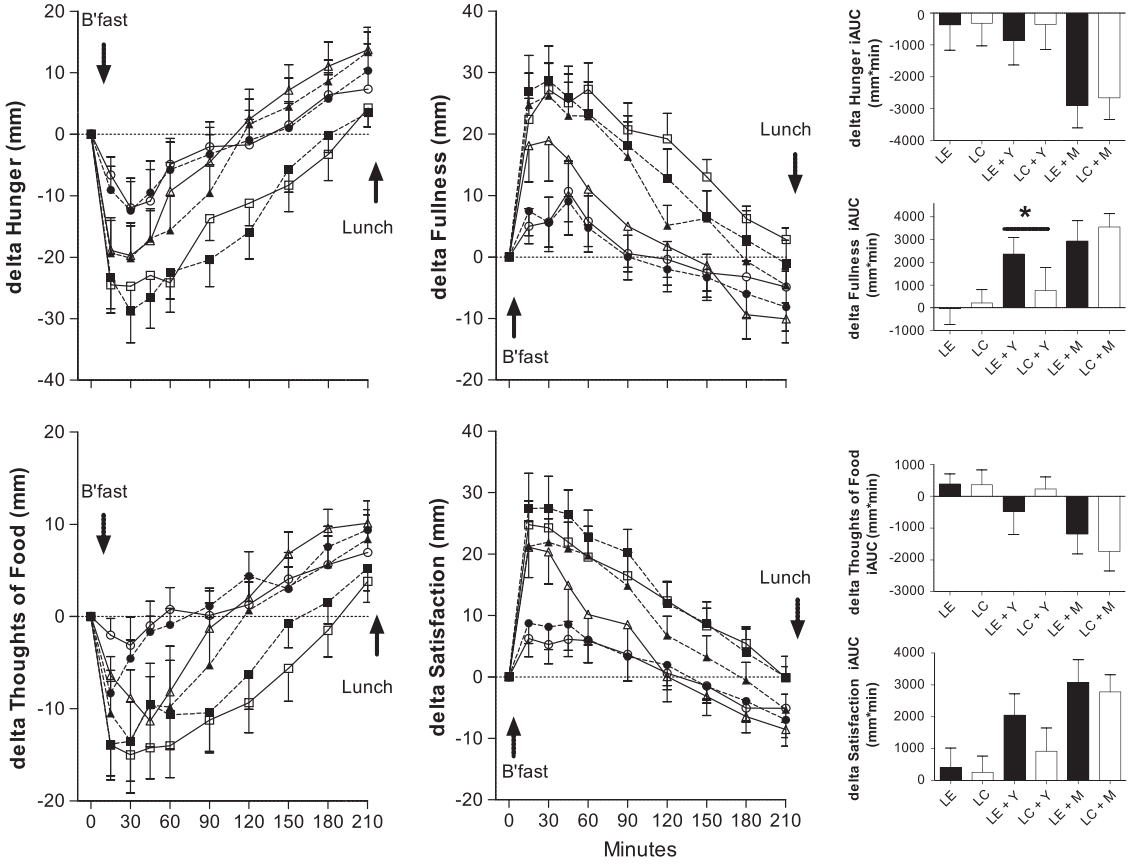

Fig. 3. Changes in hunger, fullness, current thoughts of food and satisfaction following the 6 test breakfasts, expressed as delta compared to baseline in 18 participants. Lipid emulsion (LE, ●), lipid control (LC, ○), LE + yoghurt (▲), LC + yoghurt (△), LE + muffin (■), LC + muffin (□). Incremental area under the curve (iAUC) is shown as histograms in the right hand panels. Values are presented as mean and sem. Only when administered within a semi-liquid, fermented yoghurt was there significantly greater fullness following consumption of LE compared with matched LC (*$P<0.05$). Food format as well as the energy content of the breakfasts altered appetite ratings with significantly greater changes in hunger and fullness following consumption of the solid food muffin compared with the isoenergetic semi-liquid yoghurt ($P<0.001$).

for LE than for LC ($P<0.05$). Nausea was also rated for 3 h after the breakfast but did not significantly increase following any of the 6 treatments (data not shown, $P>0.05$).

3.2.2. Hunger, fullness, TOF, satisfaction

Fig. 3 shows the change from baseline in VAS-rated hunger, fullness, current TOF and satisfaction during the 3.5 h postprandial period following each of the test breakfasts. Baseline measures were assessed following an overnight fast, and were not significantly different between study days (all, $P>0.05$). Effects of Fabuless were observed only when the emulsion was incorporated into the semi-liquid yoghurt at breakfast. Comparing each of the individual control treatments (open symbols) with the pair-matched emulsions (closed symbols), there was a greater feeling of fullness following the LE + Y (closed triangles) compared with the LC + Y (open triangles) breakfast ($P<0.05$), as well as a trend towards altered feelings of hunger/TOF/satisfaction. It was notable that the effects of the emulsion on fullness were apparent within 15 min of consumption. The calculated incremental area under the curve ($iAUC_{0-210min}$) for each of the four VAS ratings show significantly greater fullness when the emulsion was added to the yoghurt breakfast (Fig. 3, right hand panel, $P<0.05$). Conversely, there were no significant effects of the emulsion on any VAS-related measures of satiety following either of the LE or LE + M breakfasts when compared with their respective non-emulsified lipid controls ($P>0.05$).

As expected, both the energy content and format of the test breakfasts were major contributors to postprandial changes in hunger, fullness and other appetite-related assessments. The 3 non-emulsified control lipids showed a clear hierarchy of response such that suppression of hunger/TOF and enhanced fullness/satisfaction increased between the LC (0.2 MJ, open circles), the LC + Y (1.2 MJ, open triangles), and the LC + M (1.2 MJ, open squares) treatments. When yoghurt was added to LC it decreased hunger over the initial 60 min (LC vs LC + Y: 15, 30, 45, 60 min, $P<0.05$), and when the energy-matched muffin was added to LC it further suppressed hunger over a longer period of 180 min (LC vs LC + M: 15, 30, 45, 60, 90, 120, 150, 180 min, $P<0.05$). There was a similar pattern of enhanced fullness when both the yoghurt (LC vs LC + Y: 15, 30 min, $P<0.05$) and muffin (LC vs LC + M: 15, 30, 45, 60, 90, 120, 150, 180, 210 min, $P<0.05$) were added to LC. Hence, in addition to the energy content of the breakfast, food format also significantly affected the appetite ratings.

3.3. Energy intake at ad libitum lunch

Energy, protein, fat and carbohydrate (CHO) intake at the *ad lib* lunch on each of the 6 study days is shown in Fig. 4. Mean EI for all

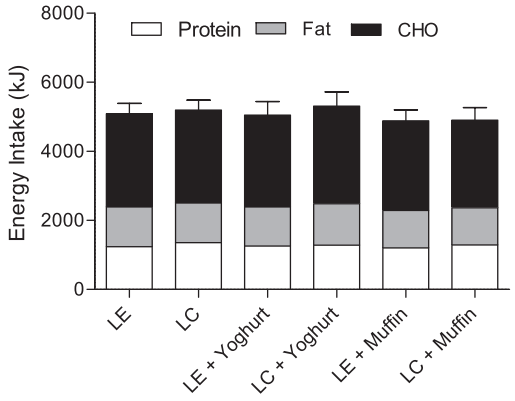

Fig. 4. Mean (sem) energy and macronutrient intake at the *ad libitum* lunch meal where participants were asked to eat until they felt comfortably full. LE, lipid emulsion; LC, lipid control; CHO, carbohydrate.

emulsion and non-emulsion treatments combined was 5069 (141 sem) kJ, and there was no significant difference between treatments (ANOVA, $P>0.05$). Review of the control treatments showed that EI following the 0.2 MJ LC breakfast was 5196 (290 sem) kJ, that there was no compensation for the addition of 1 MJ in the form of semi-liquid yoghurt (LC + Y, EI = 5308 kJ, 418 sem), and only 30% compensation for the addition of 1 MJ in solid food format muffin (LC + M, EI = 4902 kJ, 372 sem). When the control treatments were compared with the pair-matched emulsions there was a trend towards a 5% lower intake for LE + Y compared with LC + Y, but this was not a significant decrease in EI (LE + Y vs LC + Y = −5%; $P>0.05$). There was also little evidence of suppression of intake when the emulsion was consumed alone (LE vs LC = −2%: $P>0.05$) or with the breakfast muffin (LE + M vs LC + M = −0.5%; $P>0.05$). Since both response to the fixed dose preloads and *ad lib* energy intake at the lunch meal may vary between participants dependant on body weight and size, we also calculated both preload and lunch intakes as a % of predicted daily energy requirements (ER) for each participant, where ER was 1.6 times * predicted basal metabolic rate (BMR), but the outcomes were unchanged. Suppression of intake by the emulsion was greatest in LE + Y compared with LC + Y (~5% suppression of lunch intake) but this was not a significant decrease ($P>0.05$). There was also little evidence of suppression of intake when the emulsion was consumed alone (−2%: $P>0.05$) or with the breakfast muffin (−1%; $P>0.05$) compared with matched controls. There was also no significant difference in weight of food consumed or macronutrient intake between any of the emulsion and paired control lipids when analysed as absolute values or scaled to individual ER.

4. Discussion

In this study of Fabuless we found little evidence in support of suppression of appetite or food intake over the immediate 3–4 h postprandial period following consumption of the emulsion. The only significant effect was an increased feeling of fullness, and this was observed only when the emulsion was combined with a semi-liquid, fermented dairy yoghurt.

There was no evidence of similar effects when the emulsion was given either alone with water, or co-presented with a solid food item at breakfast. Interestingly none of the treatments lead to a change in eating behaviour as measured by a decrease in EI at the subsequent lunch meal.

The lack of efficacy when the emulsion was combined with yoghurt is perhaps surprising given the previous work of Burns, Livingstone and colleagues [4–6] and the fact that our current trial replicated many of the Burns' methods including lipid emulsion dose, a long inter-meal interval (3.5 h) and measurement of intake at a single subsequent free choice, buffet-style meal. Our study provided a rather more restricted buffet than the expansive meal offered by the Burns group in several of their studies, the latter often being critiqued as conducive to overconsumption and at risk of masking subtle changes in eating behaviour that may otherwise be observed between treatments [23,24]. Whilst matching the protocol of Burns et al. [4–6], it is important to note that the fixed, long inter-meal interval used in our study may have masked effects on food intake if it did not represent the time at which appetite-related signals would have initiated the lunch meal. A prolonged interval may increase hunger to a level which swamps small, differential effects of the emulsion on eating behaviour. Recent postprandial appetite studies have determined the time at which to present the lunch meal using either VAS or blood parameters such as circulating ghrelin levels, prior to commencing the study [25,26]. This has been named 'the sensitive moment in time'. Notably however using a similar protocol, in our current study of lean males, resulted in an average intake close to that observed by Burns and coworkers in their studies of lean and obese, male and females where intake was high and varied

between 4 and 8 MJ at a single meal [4–6]. The greatest effect on EI in our study also occurred when Fabuless was incorporated into yoghurt, yet this non-significant 5% decrease was far less than the previously observed ~25% decrease [4–6], which matches pharmacologically-induced suppression of eating behaviour [27]. Scaling the preloads and the energy intake to individual energy requirements did not increase the sensitivity to detect an effect of the lipid emulsions in our study.

Clearly, however, not all previous studies have shown anorectic effects of Fabuless, even when administered within a fermented yoghurt product, including later studies from the Burns group [8] and others [9,10]. The recent study by Smit and co-workers, which reported processing techniques such as thermal and shearing treatments to negate any satiety effects of Fabuless [10], led us in our current study to ensure that the emulsion did not undergo any processing. The emulsion and control lipids were given alone with water, stirred into the yoghurt treatments immediately before serving, or co-presented with the solid food muffin. None were cooked or treated in any way which may have adversely altered their structure, and hence this could not be an explanation for the unexpected lack of efficacy. Interestingly, whilst *processed* emulsion did not alter satiety or intake at a lunch (4 h) or dinner (8 h) meal, Smit was able to show that the *unprocessed* ingredient generated a delayed effect of Fabuless on food intake, although not appetite related sensations, at the second meal 8 h later. As with many previous studies, the emulsion was also given within a semi-liquid, fermented yoghurt beverage. As noted by the authors [10], this observation was not supportive of the anorectic mechanism of Fabuless being the result of a 45 min delay in oro-caecel transit [17].

Based upon the modest effects on appetite observed when Fabuless was combined with yoghurt in our study, we found little evidence to support the ileal brake as the purported mechanism by which lipid emulsions such as Fabuless may enhance satiety. Fat is likely the most important, although not the only [13], macronutrient trigger for the ileal brake, initiating a feedback loop which may inhibit upper gut motility to slow gastric emptying and intestinal transit in response to nutrients in the distal small intestine. Knutson and colleagues recently conducted an informative trial which reported a rapid and significantly increased lipid content in the jejunum 30 min after an intragastric infusion of Fabuless compared with a matched non-emulsified lipid [12]. A slower rate of lipolysis or absorption of the lipid emulsion and retention in the jejunum would explain this increased intraluminal lipid. Interestingly, *in vitro* studies mimicking gastric conditions have shown lipid emulsions to slow rates of intestinal lipolysis relative to non-emulsions, important since stimulation of the ileal brake may be dependent on the length over which lipids are hydrolysed in the GI tract [28]. Certainly infusion studies support delayed intestinal transit when/if nutrients reach the ileum [11] but whether this is achieved when emulsified lipids are orally consumed remains undemonstrated.

It would be reasonable to assume that, should delayed transit and prolonged time in the GI tract feedback to satiety, the signal would be delayed relative to a non-emulsion. GI transit of unmodified lipids is already slow, with some residence within the gut even beyond the subsequent meal [29], and activation of an ileal brake would further slow this process. It was notable in our current study that the emulsion-induced fullness was a rapid response to consumption of the yoghurt treatment, with a rapid increase by the first measured VAS time point at 15 min after the start of the breakfast meal. The delay of the absorption of fats and subsequent entry into the ileum has also been hypothesized to release peptides which signal satiety, an idea supported by studies of lipid infusion into the distal ileum [1,14,15], but again as yet unsupported by fat feeding studies.

In summary, in this study of postprandial appetite response in a group of lean men where *ad lib* energy intake was measured at a lunch meal 3.5 h later, the lipid emulsion Fabuless increased feelings of fullness only when incorporated into a semi-liquid fermented yoghurt. The increase in fullness was rapid, occurring immediately after the breakfast meal, and had dissipated 2 h later. Fabuless did not alter any measured indicators of satiety when co-presented with water or with a solid food muffin. In addition, food intake was not significantly decreased by any of the 3 emulsion treatments. We conclude from this study that the effects of Fabuless are small, the format in which the lipid emulsion is consumed influences postprandial satiety, and there is no evidence that this emulsion alters eating behaviour at a subsequent meal presented 3.5 h later.

Conflict of interest statement

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