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Small particle size lipid emulsions, satiety and energy intake in lean men

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HIGHLIGHTS

- Lipid emulsions have been proposed to suppress hunger and food intake
- Lipids delivered direct to the ileum *via* tube feeding trigger the ileal brake
- Dietary lipid emulsions are hypothesised to also trigger the brake mechanism
- We investigated whether a high phospholipid, small droplet emulsion can alter VAS-assessed appetite and *ad libitum* energy intake
- No evidence that a high phospholipid emulsion can alter eating behaviour in lean men

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ABSTRACT

Lipid emulsions have been proposed to suppress hunger and food intake. Whilst there is no consensus on optimal structural properties or mechanism of action, small particle size (small-PS) stable emulsions may have greatest efficacy. Fabuless®, a commercial lipid emulsion reported in some studies to decrease energy intake (EI), is a small-PS, 'hard' fat emulsion comprising highly saturated palm oil base (PS, 82 nm). To determine whether small-PS dairy lipid emulsions can enhance satiety, firstly, we investigated 2 'soft' fat dairy emulsions generated using dairy and soy emulsifying agents (PS, 114 nm and 121 nm) and a non-emulsified dairy control. Secondly, we investigated a small-PS palmolein based 'hard' fat emulsion (fractionated palm oil, PS, 104 nm) and non-emulsified control. This was a 6 arm, randomized, cross-over study in 18 lean men, with test lipids delivered in a breakfast meal: (i) Fabuless® emulsion (F_{EM}); (ii) dairy emulsion with dairy emulsifier (DE_{DE}); (iii) dairy emulsion with soy lecithin emulsifier (DE_{SE}); (iv) dairy control (DC_{ON}); (v) palmolein emulsion with dairy emulsifier (PE_{DE}); (vi) palmolein control (PC_{ON}). Participants rated postprandial appetite sensations using visual analogue scales (VAS), and *ad libitum* energy intake (EI) was measured at a lunch meal 3.5 h later. Dairy lipid emulsions did not significantly alter satiety ratings or change EI relative to dairy control (DE_{DE}, 4035 kJ; DE_{SE}, 3904 kJ; DC_{ON}, 3985 kJ; $P > 0.05$) nor did palm oil based emulsion relative to non-emulsified control ($PE_{DE,}$ 3902 kJ; $PC_{ON,}$ 3973 kJ; $P > 0.05$). There was no evidence that small-PS dairy lipid emulsions or commercial Fabuless altered short-term appetite or food intake in lean adults.

1. Introduction

Several studies have shown the small particle size (small-PS), 'hard fat' palm and oat oil based emulsion [2]Fabuless® (Olibra) to decrease short and medium term energy intake (EI) [1–4], although others have failed to show efficacy [5–12]. The mechanism proposed is the ileal brake [13,14]. To activate the brake emulsified oils are hypothesised to remain intact, bypassing the stomach and uptake by the proximal duodenum [15]. The delay of lipolysis and fat absorption then leads to increased exposure of fat in the distal ileum which in turn stimulates a proximal feedback loop to slow gastric emptying and small bowel motility, promotes secretion of gastrointestinal (GI) peptides, and alters hunger, fullness and food intake [13,14]. The brake mechanism is well supported by early [16–18] and more recent enteral feeding studies where small amounts of fat infused directly into the ileum altered appetite response [14,19,20]. Whether this can be

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achieved when protected lipid/water emulsions are consumed in the diet has yet to be convincingly demonstrated. Notably there is also evidence of a duodenal/jejunal brake [21], although effects may be less potent [22].

Emulsion structure directs response of the GI tract and in turn digestion rate and site [23,24], and is highly likely to alter the brake effect. The principal of oro-ileal delivery by a high phospholipid (PL) emulsion hinges on protection of central core lipids by the surrounding surface polar lipids, which may alter the rate at which core lipids are hydrolysed [25]. Hence composition and modification of both core and polar lipids may alter activation of the brake. PLs in particular have been shown to slow lipid breakdown by inhibiting the activity of lipases at the lipid/water interface by a decrease in physical contact between the lipid and the enzyme [26]. Whilst findings from Fabuless trials remain unconvincing, a recent dietary trial investigating a different high polar lipid fractionated oat oil as emulsifying agent reported increased short-term satiety [27] with evidence of increased circulation of satiety-related GI peptides. In addition, a number of recent trials have now shown small-PS emulsions to alter various aspects of satiety and food intake [19,28,29] with some evidence of greater efficacy than large-PS lipid emulsions [19,28], although again effects can be inconsistent [29]. Maljaars showed that small-PS lipid droplets significantly altered gastric emptying and satiety *versus* large-PS droplets [19], although effects were observed during infusion into the duodenum rather than ileum. Similarly, in a sophisticated magnetic resonance imaging (MRI) feeding study, Hussein and colleagues showed that decreasing fat droplet size of a plant-based emulsion could also slow gastric emptying, increase water content within the small intestine (SI), and in turn decrease short term energy intake [28]. Increased intragastric stability, which was achieved by adding a locust bean gum as a 'thickener' to prevent lipid layering, creaming and coalescence within the stomach, also suppressed food intake even when a large droplet emulsion was consumed.

This led us in the current trial to investigate whether specific features of small-PS lipid emulsions promote changes in postprandial appetite response and eating behaviour when consumed within a meal. Since lipid characteristics such as fatty acid (FA) composition, physical structure properties (*e.g.,* solid/liquid at room temperature) and stability may alter appetite-related outcomes, we compared 2 small-PS emulsions with differing physical characteristics. The test emulsions were small-PS animal-origin 'soft' fat (dairy) and plant-origin 'hard' fat (palm) lipids, emulsified using dairy or soy PLs.

2. Participants and methods

2.1. Participants

Lean male volunteers (BMI 18–25 kg/m^2), aged 18–55 years and healthy by self-report were enrolled into this intervention trial. Recruitment was carried out in Auckland through news paper and electronic advertisement. For screening, participants came fasted (overnight) to the appetite research centre at the University of Auckland Human Nutrition Unit (HNU) where body weight, height, waist circumference and blood pressure were measured. Key exclusion criteria included self-reported history of obesity or eating disorders, current cigarette smoker or restriction diet, diabetes, cardiovascular disease including hypertension, and any other significant metabolic, endocrine or GI disease. Eligible participants were free of medications known to influence appetite or weight regulation. Written consent was obtained from each of the participants, and ethical approval for this study was obtained from the Northern Regional Ethics Committee, Auckland, New Zealand. The trial was registered on the Australia New Zealand Clinical Trial Registry, international trial #ACTRN12609000853246.

2.2. Study design

Dairy derived lipid emulsions and matched controls were administered at breakfast to assess short-term appetite responses and *ad libitum* EI at a subsequent lunch meal. All participants attended the HNU on 6 separate occasions and were randomly allocated to study treatment. Between each visit they returned home for a washout period of at least 7 days during which time they were free to resume usual diet and exercise patterns. Twenty four hours prior to each study day, participants were asked to abstain from alcohol, avoid significant change in habitual diet and strenuous physical activity. To ensure compliance on pre-treatment days, participants recorded 24 h dietary intake and exercise level (time spent sitting, standing, screen activities, mild-moderate activity or vigorous/strenuous activity).

2.3. Study procedures

Standardised protocols were applied based on recommended methods of Blundell et al., [30] and previous appetite trials conducted at HNU [6,31]. On each study day participants were asked to avoid morning exercise and to fast (water only) from 8:00 pm on evening prior. Upon arrival, body weight was measured with the participant lightly clad (Seca, Model 708, Germany) and 250 mL of water was consumed. A diet and activity questionnaire was completed and adverse events (AEs) during the washout period recorded. Height was measured on a single occasion at the screening visit (Seca, model 222, Germany). Baseline VAS (visual analogue scales) were completed to rate feelings of hunger, fullness, satisfaction and current thoughts of food (TOF) prior to breakfast. The test breakfast was served at 08:30 am and participants were asked to consume the meal in full but at their own pace within 15 min. No further foods were consumed throughout the morning and the participants remained within the HNU, during which time repeat VAS ratings were measured periodically prior to lunch. 250 mL of water was served at 10:30 am. The lunch meal was served at 12:15 pm, with participants seated within individual dining booths. The timing of the lunch meal was based on previous Fabuless trials which showed effects on appetite and/or food intake at 3.5 h [6] and 4 h [1–3] following the preload. Participants were asked to eat until they felt comfortably full. No distractions were allowed during the 45 min lunch period. VAS ratings were measured over a further 2 h after completion of the lunch meal, with 150 mL of water served at 2:00 pm. Immediately after the breakfast and the lunch meal participants rated pleasantness, visual appeal, smell, taste, aftertaste and overall palatability of the meals on separate 100-mm VAS. Participants remained at the HNU throughout each study day and were allowed to use laptop computers, read or undertake other similar sedentary activities but were not allowed to sleep. The daily study protocol showing the timing of the breakfast and the *ad lib* lunch is shown in Fig. 1.

2.4. Lipid treatments

The 6 lipid treatments comprised 4 lipid plus water emulsions (Fabuless®, 2 dairy lipid; 1 palm oil lipid) and 2 matched non-emulsified controls. Dairy PL (PC700, phospholipid concentrate 700; Fonterra Co-operative Group, New Zealand, 20% of total lipid) and soya bean lecithin (American Lecithin Company, CT, USA; 20% of total lipid) were used to emulsify the lipid and water (ratio 30:70) treatments. PS of all emulsions was matched as closely as possible to the commercial lipid emulsion Fabuless®, (Table 1), and all were very small-PS lipid and water emulsions. The 6 breakfast treatments were (i) Fabuless® emulsion (F_{EM}); (ii) dairy emulsion with dairy emulsifier (DE_{DE}) matched for PS to Fabuless®; (iii) dairy emulsion with soy lecithin emulsifier (DE_{SE}) matched for PS to Fabuless®; (iv) dairy control (DC_{ON}), not emulsified; (v) palmolein emulsion with dairy emulsifier (PE_{DE}) matched for PS and FA composition to Fabuless®; (vi) palmolein control (PC_{ON}) not emulsified, matched for FA composition to Fabuless®. Since