Complaint to TGA: Blackmores Ltd ARTG: 285746 - Metabolic C12

Summary:
This complaint deals with the promotion of a weight loss product, Impromy Metabolic C12. The product is said to have been developed in collaboration with the CSIRO as part of the Impromy health improvement program. This program is said to assess weight and risk factors such as cholesterol, blood pressure and blood glucose, and includes meal replacements, high protein meals and ongoing support by trained Impromy. See screen shot below taken 19/03/2019.

https://www.impromy.com/metabolic-c12/

My concern is that the product, Impromy Metabolic C12 is also being advertised in isolation with claims on the pack and numerous web sites that I allege breach many provisions of the Therapeutic Goods Advertising Code (no 2) 2018 (the Code). Screen shots taken 19/03/2019 are appended.

These advertisements target vulnerable people who are overweight or obese. As such, I believe this complaint must be accorded a higher priority than the ‘low’ priority the TGA assigns to most complaints.

This issue has attracted media attention: “CSIRO profiting from weight loss pill with no scientific backing”.

Complaint detail:
Product name: Metabolic C12; ARTG: 285746 (Public summary attached)
Sponsor: Blackmores Ltd, PO Box 1725, WARRIEWOOD, NSW, 2102
Ingredient: Lauric acid 500 mg per soft gel capsule
Advertisement type: Internet.

Where did it appear:
- https://www.impromy.com/metabolic-c12/
- https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop
- Etc.
Complaint to TGA: Blackmores Ltd ARTG: 285746 - Metabolic C12

Date seen: 19 March 2019

Claims:

On the pack (and numerous advertisements)

- Clinically tested natural supplement
- Helps to:
  - Stimulate metabolic function
  - Assist weight loss by controlling hunger.
- Developed & Clinically Tested by the University of Adelaide

I allege these claims breach s.9 of the Code, Advertising for therapeutic goods must satisfy the following:

(a) any claims made in the advertising are valid and accurate, and all information presented has been substantiated before the advertising occurs; and
(b) it is truthful, balanced and not misleading or likely to mislead, including in its claims, presentations, representations and comparisons; and
(d) if the goods are included in the Register— it is consistent with the entry for the therapeutic goods in relation to that inclusion.

First, the ‘Clinically tested’ claim is invalid as it relates to a small, short-term, pilot study (appended) that investigated energy intake; not weight loss. The claim, “Helps to assist weight loss by controlling hunger” is equally invalid as the study did not investigate weight loss.

Second, the advertisement is inconsistent with the ARTG indication (public summary appended) which states,

“May aid or assist weight loss by suppression of appetite in conjunction with (or as part of) a kilojoule/calorie-controlled eating plan”.

The latter important statement is ignored.

In addition, the claim, “Developed & Clinically Tested by the University of Adelaide” is a breach of s.16(3)(a)(ii) and (c)(ii) of the Code (endorsements) because it fails to spell out whether the organisation, or employee, has received, or will receive, any valuable consideration for the endorsement.

Furthermore, I allege that the various advertisements below breach the following sections of the Code:

s.10(ii) by exaggerating product efficacy or performance, e.g. “A breakthrough NEW natural metabolic supplement” (many);

s.10(d)(i) by claiming “Side effect free”, SS12

s.15(2)(a) because scientific or clinical terminology must be appropriate, clearly communicated and able to be readily understood by the audience to whom it is directed, and the graph shown in SS2 fails to label the y axis of graph and does not display the lower error bars;

s.15(3)(b) because the University of Adelaide study is not sufficiently identified to enable consumers to access it (many).

s.26(1) because an advertisement for therapeutic goods containing any claim relating to weight management must balance the claims with the need for a healthy energy-controlled diet and physical activity (several advertisements lack this caveat, e.g. SS3).

There are also additional Code breaches which I will leave to the advertisers and the TGA to identify.
Complaint to TGA: Blackmores Ltd ARTG: 285746 - Metabolic C12

Screen Shots (taken 19/03/2019)

Pack shot
What is Metabolic C12?

A breakthrough NEW natural metabolic supplement.

Metabolic C12 is a clinically tested, soft-gel capsule supplement which helps to:

✔ Stimulate metabolic function
✔ Assist weight loss by controlling hunger

Developed & Clinically Tested by
the University of Adelaide

MADE FROM AN ALL-NATURAL EXTRACT

Metabolic C12 is completely natural, Gluten
Free and Dairy Free. It contains:

✔ NO caffeine
✔ NO stimulants
✔ NO flavours
✔ NO Artificial Colours

SS1 [https://www.impromy.com/metabolic-c12/](https://www.impromy.com/metabolic-c12/)
How Does Metabolic C12 Work?

Impromy Metabolic C12 works by enhancing the natural metabolic processes that are important to regulate your appetite, particularly around meal times.

When these processes are kick-started before the beginning of a meal, the body senses these signals, and the outcome is that you will feel full after consuming less calories / kilojoules.

In placebo controlled studies, oral ingestion of Metabolic C12 resulted in **13-18% less energy intake** at main meals*

SS2 [https://www.impromy.com/metabolic-c12/](https://www.impromy.com/metabolic-c12/)

Complaint to TGA: Blackmores Ltd ARTG: 285746 - Metabolic C12

<table>
<thead>
<tr>
<th>Description</th>
<th>Ingredients</th>
<th>Usage</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Always read the label, use only as directed. For adults only. Keep out of reach of children. Not suitable for pregnant or breastfeeding women or children under 16 years of age.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Complaint to TGA: Blackmores Ltd ARTG: 285746 - Metabolic C12

**IMPROMY Metabolic C12 30 Capsules**

Be the first to review this product

**SKU: 23108**

**$19.99**

Metabolic C12 helps to stimulate metabolic function and may assist weight loss by controlling hunger.

Always read the label. Follow the directions for use. Vitamins and supplements may be of assistance if dietary intake is inadequate.


**How Does Metabolic C12 Work?** Impromy Metabolic C12 works by enhancing the natural metabolic processes that are important to regulate your appetite, particularly around meal times. When these processes are kick-started before the beginning of a meal, the body senses these signals, and the outcome is that you will feel full after consuming less calories / kilojoules.

<table>
<thead>
<tr>
<th>Product</th>
<th>Impromy Metabolic C12 30 Capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand</td>
<td>Impromy</td>
</tr>
<tr>
<td>Category</td>
<td>Supplements</td>
</tr>
<tr>
<td>Dosage Form</td>
<td>Capsule, soft</td>
</tr>
</tbody>
</table>

**Impromy Flexi Metabolic C12 30 Capsules**

Impromy Metabolic C12 works by enhancing the natural metabolic processes that are important to regulate your appetite, particularly around meal times.

**$18.99**

**Save** $1.00

**ADD TO CART**

[Description](https://www.goodpricepharmacy.com.au/impromy-metabolic-c12-30-capsules)

Impromy Metabolic C12: a breakthrough new natural metabolic supplement. Metabolic C12 is a clinically tested, soft-gel capsule supplement which helps to:

- Stimulate metabolic function
- Assist weight loss by controlling hunger

- Developed & Clinically Tested by the University of Adelaide.
SS6 https://www.facebook.com/impromyweightloss/posts/%EF%B8%8F-introducing-metabolic-c12-a-breakthrough-new-natural-metabolic-supplement-deve/1586660124741374/
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Metabolic C12

- Developed by researchers at Adelaide University, multiple clinical trials
- Stimulates metabolic function
- Assists weight loss by controlling hunger
- Initiates gut constriction and slows gastric emptying
- 100% natural – no caffeine or stimulants
  - No adverse side effects
- Lauric acid (500mg) edium Chain Triglyceride
- Results in decreased energy intake (13% in clinical trials)
- 3 capsules 15-30 mins before main meal (max dosage)

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SS8  https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop

SS9  https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop
Tests showed

less energy intake at meal times!

OUTSTANDING RESULTS!

SS10 https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop

SS11 https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop
It is totally natural - side-effect, and stimulant free!

SS12 https://www.youtube.com/watch?v=n0Ce-G3_1bU&app=desktop
**Public Summary**

**Summary for ARTG Entry:** 285746 Metabolic C12 soft gel capsule

**ARTG entry for** Medicine Listed  
**Sponsor** Blackmores Ltd  
**Postal Address** PO Box 1725, WARRIEWOOD, NSW, 2102 Australia  
**ARTG Start Date** 15/02/2017  
**Product category** Medicine  
**Status** Active  
**Approval area** Listed Medicines

**Conditions**

Colouring agents used in listed medicine for ingestion, other than those listed for export only under section 25 of the Act, shall be only those included in the list of 'Colourings permitted in medicines for oral use'.

The sponsor shall keep records relating to this listed medicine as are necessary to: (a) Expedite recall if necessary of any batch of the listed medicine,  
(b) Identify the manufacturer(s) of each batch of the listed medicine. Where any part of or step in manufacture in Australia of the listed medicine is sub-contracted to a third party who is not the sponsor, copies of relevant Good Manufacturing Practice agreements relation to such manufacture shall be kept.

The sponsor shall retain records of the distribution of the listed medicine for a period of five years and shall provide the records or copies of the records to the Complementary Medicines Branch, Therapeutic Goods Administration, upon request.

The sponsor of the listed medicine must not, by any means, intentionally or recklessly advertise the medicine for an indication other than those accepted in relation to the inclusion of the medicine in the Register.

All reports of adverse reactions or similar experiences associated with the use or administration of the listed medicine shall be notified to the Head, Office of Product Review, Therapeutic Goods Administration, as soon as practicable after the sponsor of the goods becomes aware of those reports. Sponsors of listed medicines must retain records of such reports for a period of not less than 18 months from the day the Head, Office of Product Review is notified of the report or reports.

The sponsor shall not supply the listed medicine after the expiry date of the goods.

Where a listed medicine is distributed overseas as well as in Australia, product recall or any other regulatory action taken in relation to the medicine outside Australia which has or may have relevance to the quality, safety or efficacy of the goods distributed in Australia, must be notified to the National Manager Therapeutic Goods Administration, immediately the action or information is known to the sponsor.

**Products**

1. **Metabolic C12 soft gel capsule**  

**Product Type** Single Medicine Product  
**Effective date** 26/09/2018

**Permitted Indications**

**Indication Requirements**

No Indication Requirements included on Record

**Standard Indications**

May aid or assist weight loss by suppression of appetite in conjunction with (or as part of) a kilojoule/calorie controlled eating plan.

**Specific Indications**

Helps to stimulate metabolic function  
Helps to assist weight loss by controlling hunger

**Warnings**

Not recommended for use by pregnant and lactating women (or words to that effect).  
Adults only (or words to that effect).

**Additional Product information**

**Pack Size/Poison information**

**Pack Size** 
**Poison Schedule**

**Components**

1. Formulation 1

**Dosage Form** Capsule, soft

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This is not an ARTG Certificate document.  
The onus is on the reader to verify the current accuracy of the information on the document subsequent to the date shown.  
<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Identification</td>
<td></td>
</tr>
<tr>
<td><strong>Active Ingredients</strong></td>
<td></td>
</tr>
<tr>
<td>lauric acid</td>
<td>500 mg</td>
</tr>
</tbody>
</table>
Original article

Acute oral administration of lauric acid reduces energy intake in healthy males

Kate L. Feltrina, Ixchel M. Brennan, Thomas Rades, Michael Horowitz, Christine Feinle-Bisset

School of Pharmacy, University of Otago, Dunedin, New Zealand
NHMRC Centre of Research Excellence in Translating Nutritional Science to Good Health, Adelaide, South Australia, Australia
University of Adelaide Discipline of Medicine, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Abstract

Background and aims: We have established that acute intraduodenal infusion of the fatty acid, lauric acid (C12), markedly reduces energy intake in healthy subjects in the absence of adverse effects. The aim of this study was to investigate the hypothesis that increasing doses of orally ingested C12 would result in a dose-related suppression of appetite and subsequent energy intake at breakfast and lunch.

Methods: 14 healthy men were studied on four separate occasions in double-blind, randomised fashion. Following ingestion of C12 (2 g (77 kJ), 4 g (153 kJ), or 6 g (230 kJ)) or control, energy intake at breakfast (30 min after C12 ingestion), perceptions of appetite, nausea and bloating (for 180 min following breakfast), and energy intake at lunch (180 min after breakfast), were measured.

Results: C12 ingestion did not induce nausea or bloating. While there was no effect of C12 on energy intake at breakfast, energy intake at lunch was reduced significantly after ingestion of both C12(2 g) (by 13.7%, P < 0.05) and C12(6 g) (by 18.1%, P < 0.01) compared with control, and tended to be less (by 8.7%, P = 0.1) following C12(4 g). Total energy intake (breakfast + lunch + C12 dose) was less following ingestion of C12(6 g) compared with control (by 7.8%, P < 0.05) (kJ; control: 8256 ± 297, C12(2 g): 7905 ± 269, C12(4 g): 8443 ± 421, C12(6 g): 7611 ± 384).

Conclusion: Acute administration of oral C12 reduces energy intake in lean humans.

1. Introduction

While numerous pharmacological treatments for obesity have been developed, most of these therapies result in only modest weight loss of 5–10%, that is often not maintained in the longer-term, and several drugs have a high prevalence of adverse effects, with both rimonabant and sibutramine recently withdrawn from the market. Moreover, these drugs do not take advantage of the pivotal role of the gastrointestinal (GI) tract in the regulation of energy intake in response to nutrients, or body weight following Roux-en-Y gastric bypass surgery. The only currently available drug that claims to facilitate weight loss by a GI mechanism is orlistat (Xenical), which inhibits GI lipases and, thus, impairs fat digestion and absorption. However, this is associated with unpleasant adverse effects, and we have established that orlistat has acute effects on GI function, which favour an increase, rather than a decrease, in energy intake and also compromise glycaemic control.

The presence of nutrients, especially fat, in the small intestine stimulates the release of gut hormones, including cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1) and peptide YY (PYY), and suppression of ghrelin. These mediates, at least in part, the effects of fat on the reduction of hunger and subsequent energy intake, and the modulation of GI motility, leading to slowed gastric emptying and improved glycaemic control. The effects of fat on appetite and GI function are mediated by their...
digestive products, free fatty acids,\textsuperscript{5,6} and the effects of fatty acids are chain length-dependent, i.e. fatty acids with a chain length of $\geq 12$ C atoms are more potent than those with a chain length of $<12$ C atoms.\textsuperscript{16,18} and lauric acid (C12) appears to also be more potent than oleic acid (C18:1).\textsuperscript{19}

Our previous studies have demonstrated that intraduodenal C12, at the small load of $0.4$ kcal/min, decreases energy intake without inducing nausea, associated with changes in upper GI function, particularly the stimulation of pyloric motility and CCK secretion.\textsuperscript{16,20} Since both the stimulation of pyloric pressures and plasma CCK are independent predictors of subsequent energy intake,\textsuperscript{3} they are likely to mediate, at least in part, the suppression of energy intake by C12. It is currently not known, whether the effects of intraduodenal C12 are evident when C12 is ingested orally, because the rate of gastric emptying of fatty acids is very small. A previous study\textsuperscript{18} has, however, demonstrated that intragastric administration of C12 suppresses antral contractions, relaxes the proximal stomach, and stimulates CCK secretion in healthy subjects. Accordingly, it is likely that orally administered C12 would produce comparable changes in GI function, associated with reductions in energy intake and bloating.

The aims of this study were, therefore, to investigate the hypothesis that oral C12 would suppress energy intake both at breakfast (30 min after C12 ingestion) and lunch (180 min after breakfast) in healthy subjects.

2. Materials and methods

The study protocol consisted of a pilot study and the main study, both of which were approved by the Royal Adelaide Hospital Research Ethics Committee, and each subject provided written, informed consent prior to their inclusion. The procedures followed in the studies were in accordance with the Declaration of Helsinki. Recruitment for the study commenced in February 2006, and data collection was completed in May 2007.

2.1. Pilot study: effects of oral ingestion of C12 on GI symptoms

As the effects of oral C12 had not been evaluated previously, it was not known whether it would be tolerated without inducing adverse effects, such as nausea. Accordingly, prior to investigating the effects of oral C12 on appetite and energy intake, a pilot study was conducted to determine the effect of increasing doses of oral C12 on GI symptoms.

2.1.1. Subjects

5 healthy, males, with a mean age of 25 ± 4 (range 19–45) years and of normal body weight for their height (BMI 22.5 ± 0.6 kg/m$^2$) were studied (Supplemental Fig. 1). All subjects were unrestrained eaters (mean score on the eating restraint part (Factor 1) of the Three Factor Eating questionnaire\textsuperscript{15} 4.6 ± 1.4 (range: 0–8)), had no known GI disease or symptoms, and were not taking any medication. No subject smoked or habitually consumed $>20$ g alcohol per day.

2.1.2. Study design

Each subject was studied on five occasions, separated by 3–10 days, to evaluate in single-blind fashion, the effects of increasing doses of oral C12 at 1 g (“C12(1 g)”), 2 g (“C12(2 g)”), 3 g (“C12(3 g)”) and 4 g (“C12(4 g)”), providing ~38 kcal, 76.5 kcal, 115 kcal and 153 kcal, respectively, or control, on perceptions of nausea and bloating. The doses of C12 were based on our previous studies, in which C12 was administered intraduodenally at infusion rates that equalled total loads of ~1–5 g,\textsuperscript{16,19,20} and a study delivering C12 into the stomach at loads of ~2–5 g.\textsuperscript{18}

2.1.3. Preparation of C12 capsules

Hydroxypropylmethylcellulose (HPMC) capsules (size 00, Capsuline Inc, Pompano Beach, FL, USA) were filled with 0.5 g C12 (Sigma–Aldrich, Milwaukee, WI, USA) each. Thus, in order to provide doses of 1, 2, 3 or 4 g C12, subjects received 2, 4, 6 or 8 capsules. Control capsules were filled with 0.5 g ascorbic acid (Chem-Supply, Gillman, SA, Australia). Each subject received 8 capsules on each day, i.e. the required number of C12 capsules to provide the dose of C12, supplemented with between 0 and 8 placebo capsules. The control day was randomised (i.e. on any of the 5 visits), however, as this was, to our knowledge, the first study of the effects or orally ingested C12, the dose of C12 was increased with each visit (starting with 1 g of C12), although the subjects were unaware of this.

2.1.4. Protocol

Subjects were instructed to maintain their normal diet between study days and refrain from vigorous exercise and alcohol intake for 24 h before each study day. Subjects attended the Discipline of Medicine at 0830 h following an overnight fast from solids and liquids from 2200 h the previous night.

Upon arrival subjects were seated in a chair and completed a visual analogue scale questionnaire (VAS) for the assessment of nausea and bloating, as well as appetite-related sensations ($t = 0$ min).\textsuperscript{2,3} Each VAS consisted of a 100-mm horizontal line, where 0 represented ‘sensation is not felt at all’ and 100 ‘sensation is felt the greatest’. Subjects were asked to place a vertical stroke on the line to indicate what they were feeling at that particular point in time. Subjects then ingested the capsules with 250 ml of water. Subsequently, VAS were administered every 15 min between $t = 15$–90 min, and every 30 min between $t = 90$–180 min. At $t = 180$ min subjects were offered a light sandwich lunch, after which they were allowed to leave the laboratory. Subjects were asked to report any adverse effects in the subsequent 24 h.

2.2. Main study: effects of oral ingestion of C12 on appetite and energy intake

2.2.1. Subjects

14 healthy males were included in the study (Supplemental Fig. 2); the number of subjects was based on power calculations derived from a previous study\textsuperscript{22}; it was calculated that with 14 subjects a 15% decrease in energy intake could be detected at $\alpha = 0.05$, with a power of 80%. Subjects had a mean age of 24 ± 1 (range 19–41) years, were of normal body weight for their height (BMI 23.2 ± 0.4 kg/m$^2$), were unrestrained eaters ($\geq 3.7$ ± 0.8 [range: 0–9]), had no known GI disease or symptoms, and were not taking medication. No subject smoked or habitually consumed $>20$ g alcohol per day. Once subjects were enrolled into the study, they were allocated a random sequence of all 4 treatments, generated using the #RAN function in Microsoft Excel, by a research officer. Both the subject, and investigator assessing outcomes (KLF), were blinded to the random allocation sequence.

2.2.2. Study design

Each subject was studied on four occasions, separated by 3–10 days, in double-blind, randomised fashion, to evaluate the effects of oral C12 at (i) 2 g (“C12(2 g)”), (ii) 4 g (“C12(4 g)”) or (iii) 6 g (“C12(6 g)”), providing ~76.5 kcal, 153 kcal or 230 kcal, respectively, or (iv) control, on appetite perceptions, nausea and bloating (from 45 min before, until 180 min after, breakfast), energy intake at breakfast (30 min after C12 ingestion) and energy intake at lunch (180 min after breakfast) (Fig. 1). As no adverse effects occurred in
the pilot study following ingestion of up to 4 g of C12 (described in the Results), 6 g was selected as the maximum dose in the ‘main study’.

2.2.3. Preparation of capsules
C12, or ascorbic acid, was filled in size 00 HPMC capsules. Since 12 capsules were required to deliver 6 g C12 (condition C12(6 g)), subjects ingested 12 capsules on each occasion; i.e. 8 C12 capsules and 4 placebo capsules for condition C12(4 g), 4 C12 capsules and 8 placebo capsules for condition C12(2 g) and 12 placebo capsules on the control day. The capsules were prepared by a co-investigator so that both the subjects and primary investigator were blinded. Subjects were unable to discriminate between the placebo and C12 capsules, by either their appearance or weight.

2.2.4. Protocol
Subjects were instructed to maintain their normal diet and refrain from vigorous exercise and alcohol intake for 24 h before each study day, and attended the Discipline of Medicine at 0830 h following an overnight fast from solids and liquids from 2200 h the previous night.

Upon arrival, subjects were seated and, at $t = -45$ min, completed a VAS22 for the assessment of appetite perceptions (hunger and fullness), as well as nausea and bloating, and then ingested the 12 capsules with 250 ml of water. At $t = -30$ and $t = -15$ min subjects completed further VAS. At $t = -15$ min, subjects were then presented with a standardised, buffet-style breakfast (Table 1) and allowed to eat freely for 15 min until they were comfortably full. VAS were administered every 15 min between $t = 0$–90 min, and every 30 min between $t = 90$–180 min (i.e. from the end of breakfast until the start of lunch). At $t = 180$ min, subjects were presented with a standardised, cold, buffet-style lunch (Table 2) and allowed 30 min to eat, while again being instructed to eat until comfortably full. The buffet meal is regularly used in our studies to quantify energy intake.24 The amount of food offered at both meals was in excess of what the subject was expected to consume. After lunch, the subject was expected to refrain from vigorous exercise and alcohol intake for 24 h before the pilot study following ingestion of up to 4 g of C12 (described in the Results), 6 g was selected as the maximum dose in the ‘main study’. The amount of food offered at both meals was in excess of what the subject was expected to consume. After lunch, the subject was expected to refrain from vigorous exercise and alcohol intake for 24 h before the pilot study following ingestion of up to 4 g of C12 (described in the Results), 6 g was selected as the maximum dose in the ‘main study’.

2.3. Statistical analysis
In the pilot study, VAS scores at $t = 0$ min were taken as baseline values, and in the main study, baseline VAS scores were calculated from the VAS obtained at $t = -45$, -30 and -15 min. In both studies, VAS scores between 0 and 180 min were analysed by repeated-measures ANOVA with time and treatment as within-

### Table 1
Composition of the buffet-style breakfast.

<table>
<thead>
<tr>
<th>Food items</th>
<th>Amount served (g)</th>
<th>Energy content (kJ)</th>
<th>Fat (g)</th>
<th>Carbohydrate (g)</th>
<th>Protein (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wholemeal bread, 2 slices</td>
<td>60</td>
<td>626</td>
<td>1.7</td>
<td>24.0</td>
<td>6.1</td>
</tr>
<tr>
<td>White bread, 2 slices</td>
<td>60</td>
<td>622</td>
<td>1.4</td>
<td>27.1</td>
<td>5.6</td>
</tr>
<tr>
<td>Crumpets</td>
<td>100</td>
<td>639</td>
<td>0.7</td>
<td>30.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Blueberry muffin</td>
<td>45</td>
<td>713</td>
<td>4.0</td>
<td>31.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Breakfast bar</td>
<td>40</td>
<td>620</td>
<td>1.8</td>
<td>29.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Strawberry yoghurt</td>
<td>200</td>
<td>966</td>
<td>6.2</td>
<td>33.8</td>
<td>9.4</td>
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<tr>
<td>Apple</td>
<td>170</td>
<td>359</td>
<td>0.2</td>
<td>21.3</td>
<td>0.5</td>
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<tr>
<td>Banana</td>
<td>120</td>
<td>430</td>
<td>0.1</td>
<td>23.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Orange</td>
<td>180</td>
<td>288</td>
<td>0.2</td>
<td>14.6</td>
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<tr>
<td>Apple juice</td>
<td>260</td>
<td>486</td>
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<td>28.6</td>
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<tr>
<td>Iced chocolate</td>
<td>630</td>
<td>2155</td>
<td>21.4</td>
<td>59.2</td>
<td>20.8</td>
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<tr>
<td>Margarine</td>
<td>20</td>
<td>516</td>
<td>13.9</td>
<td>0.1</td>
<td>0.1</td>
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<td>Vegemite</td>
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<td>119</td>
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<tr>
<td>Strawberry jam</td>
<td>30</td>
<td>327</td>
<td>0.3</td>
<td>19.5</td>
<td>0.3</td>
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<tr>
<td>Total</td>
<td>1885</td>
<td>8749</td>
<td>54.6</td>
<td>338.3</td>
<td>62.8</td>
</tr>
</tbody>
</table>

### Table 2
Composition of the buffet-style lunch.

<table>
<thead>
<tr>
<th>Food items</th>
<th>Amount served (g)</th>
<th>Energy content (kJ)</th>
<th>Fat (g)</th>
<th>Carbohydrate (g)</th>
<th>Protein (g)</th>
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<tbody>
<tr>
<td>Wholemeal bread, 4 slices</td>
<td>125</td>
<td>1304</td>
<td>3.6</td>
<td>50.0</td>
<td>12.6</td>
</tr>
<tr>
<td>White bread, 4 slices</td>
<td>125</td>
<td>1295</td>
<td>2.9</td>
<td>56.4</td>
<td>11.8</td>
</tr>
<tr>
<td>Ham, sliced</td>
<td>100</td>
<td>453</td>
<td>3.6</td>
<td>0</td>
<td>18.8</td>
</tr>
<tr>
<td>Chicken, sliced</td>
<td>100</td>
<td>677</td>
<td>7.0</td>
<td>0</td>
<td>24.6</td>
</tr>
<tr>
<td>Cheese, sliced</td>
<td>85</td>
<td>1436</td>
<td>28.3</td>
<td>0.9</td>
<td>21.9</td>
</tr>
<tr>
<td>Tomato, sliced</td>
<td>100</td>
<td>56</td>
<td>0.1</td>
<td>1.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Lettuce</td>
<td>100</td>
<td>27</td>
<td>0</td>
<td>0.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Cucumber, sliced</td>
<td>100</td>
<td>44</td>
<td>0.1</td>
<td>1.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Strawberry yoghurt</td>
<td>200</td>
<td>966</td>
<td>6.2</td>
<td>33.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Fruit salad</td>
<td>140</td>
<td>343</td>
<td>0.1</td>
<td>19.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Chocolate custard</td>
<td>150</td>
<td>662</td>
<td>5.3</td>
<td>22.7</td>
<td>4.8</td>
</tr>
<tr>
<td>Apple</td>
<td>170</td>
<td>359</td>
<td>0.2</td>
<td>21.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Banana</td>
<td>190</td>
<td>680</td>
<td>0.2</td>
<td>37.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Orange juice, unsweetened</td>
<td>500</td>
<td>800</td>
<td>5.0</td>
<td>42.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Iced coffee</td>
<td>600</td>
<td>1788</td>
<td>10.2</td>
<td>61.8</td>
<td>21.0</td>
</tr>
<tr>
<td>Water</td>
<td>600</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Margarine</td>
<td>20</td>
<td>609</td>
<td>16.4</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>20</td>
<td>310</td>
<td>6.5</td>
<td>4.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>3425</td>
<td>11,808</td>
<td>95.7</td>
<td>354.6</td>
<td>136.9</td>
</tr>
</tbody>
</table>

### Notes
- a Sunblest, TipTop, Enfield, NSW, Australia.
- b Gibbs Crumpets, Gibbs Pty Ltd, Australia.
- c R-time muffin bar, Kellogg’s (Aust) Pty Ltd, Melbourne, VIC, Australia.
- d Uncle Tobys Sports Plus Breakfast Bar, The Uncle Tobys Company, Sydney, NSW, Australia.
- e Yoplait, National Foods Ltd, Docklands, VIC, Australia.
- f Poptop apple drink, P & N Beverages Australia Pty Ltd, Sydney, NSW, Australia.
- g Pura Classic chocolate, National Foods Ltd, Docklands, VIC, Australia.
- h Flora, Unilever Australasia, Australia.
- i Kraft Vegemite, Kraft Foods Ltd, Australia.
- j Heinz strawberry jam, Heinz Wattie’s Ltd, Australia.
are presented as means ± SEM. Dose–response relationships between hunger, fullness and energy intake and the amount of C12 administered (i.e., 0, 2, 4 or 6 g) were determined using linear associations by calculating correlation coefficients adjusted for repeated measures.

3. Results

3.1. Pilot study

All 5 subjects completed the four study days and tolerated the experimental conditions well. No nausea or bloating, or any other adverse effect, was reported by any subject following ingestion of any dose of C12, or control (for up to 24 h later). For 180 min after ingestion of C12, scores for nausea and bloating did not change from baseline (Fig. 2), hence, oral C12 at 1–4 g was well tolerated.

3.2. Main study

All 14 subjects completed the four study days and tolerated the experimental conditions well.

3.2.1. Appetite perceptions and gastrointestinal symptoms

3.2.1.1. Hunger. Following breakfast, scores for hunger decreased when compared with baseline with all treatments \((P < 0.001)\) (Fig. 3(A)). Subsequently, hunger increased slowly between \(t = 0–180\) min. While there was no significant effect of treatment on hunger, mean values were lowest following C12(2 g) and C12(6 g). There was a significant effect of time for hunger \((P < 0.001)\), such that hunger was greater compared with \(t = 0\) min (i.e. end of breakfast) following control from \(t = 75\) min \((P < 0.05)\), C12(4 g) from \(t = 60\) min \((P < 0.05)\), and C12(6 g) from \(t = 75\) min \((P < 0.05)\), until \(t = 180\) min (i.e. start of lunch). At \(t = 180\) min, scores for fullness were still greater than at baseline following all treatments \((P < 0.01)\).

3.2.1.2. Fullness. Following breakfast, scores for fullness increased when compared with baseline with all treatments \((P < 0.001)\) (Fig. 3(B)). Subsequently, fullness decreased slowly between \(t = 0–180\) min. While there was no significant effect of treatment on fullness, mean values were higher following C12(6 g) between \(t = 0–180\) min. There was a significant effect of time for fullness \((P < 0.001)\), such that fullness was less compared with \(t = 0\) min (i.e. end of breakfast) following control and C12(2 g) from \(t = 45\) min \((P < 0.05\) for both), C12(4 g) from \(t = 30\) min \((P < 0.05)\), and C12(6 g) from \(t = 75\) min \((P < 0.05)\), until \(t = 180\) min (i.e. start of lunch). At \(t = 180\) min, scores for fullness were still greater than at baseline following all treatments \((P < 0.01)\).

3.2.1.3. Nausea and bloating. There was no effect of treatment on either nausea (Fig. 3(C)) or bloating (Fig. 3(D)). There was a significant effect of time for bloating \((P < 0.001)\), but not nausea. Following breakfast, bloating increased slightly with all treatments \((P < 0.05)\). Subsequently, bloating decreased and was less compared with \(t = 0\) min (i.e. end of breakfast) following control from \(t = 30\) min \((P < 0.05)\), C12(2 g) and C12(4 g) from \(t = 15\) min \((P < 0.001)\), and C12(6 g) from \(t = 60\) min \((P < 0.05)\). From \(t = 90\) min, there were no differences compared with baseline scores.

3.2.2. Energy intake

3.2.2.1. Breakfast. There was no effect of treatment on either energy intake or the weight (Table 3) or macronutrient composition (data not shown) of food consumed.

3.2.2.2. Lunch. There was a significant effect of treatment on energy intake \((P < 0.05)\) (Table 3). Both C12(2 g) and C12(6 g)
decreased energy intake when compared with control ($P < 0.05$), C12(2 g) by a mean of 565 kJ (13.7%) and C12(6 g) by a mean of 758 kJ (18.1%), while the difference between C12(4 g) and control (358 kJ; 8.7%) was not significant ($P = 0.1$). There were no significant differences between C12(2 g), C12(4 g) and C12(6 g). There was no significant relationship between energy intake with the amount of C12 administered, or with scores for hunger and fullness at $t = 180$ min.

There was no effect of treatment on the weight (Table 3) or macronutrient composition (data not shown) of food consumed.

3.2.2.3. Total energy intake (breakfast + lunch + C12 dose).

There was a significant effect of treatment on total energy intake ($P < 0.05$) (Table 3). C12(6 g) decreased energy intake when compared with both control and C12(4 g) (both $P < 0.05$), while there was no difference between C12(2 g) and C12(6 g), or between control, C12(2 g) and C12(4 g). There was a net mean reduction in energy intake by 645 kJ (7.8%) following C12(6 g) ($P < 0.05$) and by 351 kJ (4.3%) following C12(2 g), although this was not statistically significant, but not following C12(4 g). There was no significant relationship between energy intake with the amount of C12 administered.

There was no effect of treatment on the weight (Table 3) or macronutrient composition (data not shown) of food consumed.

4. Discussion

This study has established in healthy, lean humans that, when ingested orally, acute administration of C12 has the capacity to
Table 3 Energy intake (kJ) and weight of food consumed (g) following oral ingestion of control or lauric acid (C12) at 2, 4, and 6 g, at breakfast, lunch and ‘total’ (breakfast + lunch + C12 dose) food consumed.*

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>C12(2 g)</th>
<th>C12(4 g)</th>
<th>C12(6 g)</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td>4024 ± 211</td>
<td>4162 ± 163</td>
<td>4416 ± 218</td>
<td>3907 ± 243</td>
<td>NS</td>
</tr>
<tr>
<td>Weight of food (g)</td>
<td>826 ± 50</td>
<td>821 ± 27</td>
<td>903 ± 63</td>
<td>768 ± 56</td>
<td>NS</td>
</tr>
<tr>
<td>Lunch</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td>4232 ± 151</td>
<td>3667 ± 283</td>
<td>3874 ± 315</td>
<td>3474 ± 237</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Weight of food (g)</td>
<td>1040 ± 96</td>
<td>918 ± 74</td>
<td>1034 ± 77</td>
<td>949 ± 99</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (kJ)</td>
<td>8256 ± 297</td>
<td>7965 ± 269</td>
<td>8443 ± 421</td>
<td>7611 ± 384</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Weight of food (g)</td>
<td>1866 ± 134</td>
<td>1739 ± 86</td>
<td>1937 ± 121</td>
<td>1717 ± 141</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Data are means ± SEM (n = 14).

The suppression of energy intake, and this does not reflect an adverse effect. C12, when ingested 30 min before breakfast, did not affect energy intake at breakfast, but energy intake at lunch, consumed 225 min later, was decreased by ~13.7%, 8.7% and 18.1% following C12 doses of 2, 4 and 6 g, respectively, when compared with control. Furthermore, total energy intake (breakfast + lunch + C12 dose) was reduced following 6 g of C12, compared with control, by ~7%. Hence, the magnitude of suppression of energy intake resulting from acute administration of C12 is marked and would be of substantial significance if maintained during chronic administration.

While the current study did not assess the effects of oral C12 on GI function, we have established that intraduodenal C12 potently stimulates pyloric motility and the release of CCK, GLP-1 and PY, and others have shown that intragastric C12 (~2.5 g) modulates gastric motility and stimulates both CCK secretion and gallbladder contraction. Given that we have recently identified both pyloric pressures and plasma CCK as independent determinants of energy intake in response to small intestinal nutrients, these parameters are likely, at least in part, to also underlie the effects of oral C12.

While the suppression of energy intake by C12 was not clearly dose-related, C12 effectively reduced energy intake following oral ingestion, although it is uncertain why 4 g of C12 did not suppress energy intake significantly. It is of interest that the reduction in energy intake by C12 was not associated with a change in the amount (g) of food consumed, that is, subjects consumed a less energy-dense meal. Furthermore, while both 2 g and 6 g of C12 suppressed energy intake, this occurred in the absence of significant changes in appetite perceptions, as was the case following intraduodenal C12 administration. While assessment of appetite by VAS has limitations, it is possible that a reduction in appetite perceptions may not be required for the effects of C12 on energy intake. However, this may represent a type-2 error, considering there were trends for C12 at 6 g to reduce hunger and increase fullness more than the other doses, and the inclusion of more subjects may have resulted in significant differences.

Previous studies have demonstrated that intragastric or intraduodenal C12 stimulated CCK secretion within ~15–30 min; hence, the current study assessed whether energy intake would be reduced 30 min following C12 ingestion. This was not the case, and it is likely that very little C12 would have emptied within 30 min, since a recent study reported marked slowing of gastric emptying following intragastric administration of a 40 g C18 emulsion, such that only ~10 g of C18 had emptied from the stomach after 240 min; therefore, it is not surprising that energy intake at breakfast was not reduced. Accordingly, 225 min following oral C12, it would be expected that all of the C12, at all doses, and probably the majority of the breakfast meal, would have emptied from the stomach, stimulating maximal gut hormone concentrations; hence, the marked reduction in energy intake at lunch. Moreover, the emptying of most of the breakfast meal from the stomach would have potentiated the suppressive effects of C12 on energy intake at lunch.

A number of limitations of our study design warrant discussion. The ad libitum breakfast may have encouraged subjects to overeat and consequently blunted the suppressive effect of C12 on energy intake at lunch. Administering a smaller, standardised breakfast may have potentially revealed greater suppression of energy intake at lunch. The rate of gastric emptying of C12 was not controlled for, or measured, hence, there may have been inconsistencies in the delivery of C12 from the stomach into the small intestine between subjects. C12 is solid at room temperature, and in any form (solid or liquid), does not dissolve or break down well in water. This may have caused the C12 not to empty into the small intestine at a constant rate, thus, the lack of clear dose-related suppression of energy intake. Our study only included healthy males, thus we cannot, at this stage, extend our conclusions to females, although major differences in the response seem unlikely. Furthermore, our findings require confirmation in the obese, given they are the target population. Finally, exposure of the small intestine to fatty acids may lead to transient mucosal damage. However, these effects appear to increase with the fatty acid chain length, so that C18 fatty acids are more potent than C12, although these studies were performed in 1-day to 1-month old piglets, thus, the relevance of the findings to humans is uncertain, and acute oral ingestion of C12 is arguably unlikely to produce any permanent cytotoxic effects to small intestinal mucosa, considering that damage to the intestinal epithelium by fatty acids would be comparable to that observed following ‘normal’ meal digestion and absorption. Since C12 is a saturated fatty acid and there is a rationale to reduce saturated fat intake, because of potential detrimental health effects, including increased plasma cholesterol, it is important to recognise that the evidence for this is inconclusive, and that C12 in fact decreases total cholesterol to HDL ratio. In any case, if C12 induces weight loss in obese subjects, the resulting long-term improvement in the plasma lipid profile would almost certainly outweigh any potential detrimental effect of C12. Nevertheless, the effects of longer-term exposure of C12 on the small intestinal mucosa and on triglyceride profiles warrant further evaluation.

In summary, this study has established that acute oral ingestion of C12 has the capacity to reduce energy intake, without inducing adverse effects, in doses as low as 2 g, indicating potential for C12 as a nutrient-based treatment for weight loss in obesity. Studies are now required to establish whether the acute suppression of energy intake by oral C12 is sustained during chronic administration, and associated with weight loss, in the obese.

Sources of funding

KLF was supported by a Dawes Postgraduate Research Scholarship provided by the Royal Adelaide Hospital, and IMB by a Dawes Postgraduate Research Scholarship provided jointly by the Royal Adelaide Hospital and the University of Adelaide. CFB was supported by a National Health and Medical Research Council of Australia (NHMRC) Career Development Award (grant no. 299074, 2004–2009) and an NHMRC Senior Research Fellowship (grant no.
G27002, 2010–2014). The study was supported by an NHMRC project grant to CFB (grant no. 565311, 2009–2012).

Conflict of interest

None of the authors had a conflict of interest.

Acknowledgements

Statement of authorship: CF-B and TR conceived the project and designed the overall research plan, KLF and IMB conducted the research, CF-B and KLF analysed data and performed the statistical analysis, KLF, IMB, TR, CF-B and MH contributed to data interpretation, KLF, CF-B and MH wrote the paper, CF-B had primary responsibility for the final content. All authors read and approved the final manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.clnme.2014.01.004.

References