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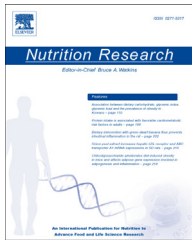

Encapsulation of lipids as emulsion-alginate beads reduces food intake: a randomized placebo-controlled cross-over human trial in overweight adults

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ABSTRACT

The objective of this study was to investigate the efficacy of lipid emulsions encapsulated in calcium-alginate beads in reducing food intake and appetite sensations. These emulsion-alginate beads were ingested in a yogurt (active) and compared to an equienergetic yogurt containing nonencapsulated nutrients with comparable sensory properties (control) in a randomized placebo-controlled trial with crossover design. Thirty-three healthy overweight volunteers (mean age: 43 years; body mass index: 27.7 kg/m^2; 14 male) received the 2 treatments. Test days started with a standardized small breakfast (t = 0) followed by an active or control yogurt (t = 90 minutes). Appetite sensations and gastrointestinal symptoms were monitored prior to and after consumption of the yogurt, and food intake was measured during ad libitum pasta meal consumption (t = 210 minutes). The hypothesis for this study was that delayed release of encapsulated lipids suppresses appetite sensations and reduces food intake. Food intake was significantly reduced with 51 ± 20 kcal (213 ±84 kJ) (P = .016) after intake of the active yogurt (770 ± 38 kcal (3222± 159 kJ)) compared to the control (821 ± 40 kcal (3435 ±167 kJ)). The approach that we chose is promising to reduce food intake and could contribute to the development of an easy-to-use product for weight management.

1. Introduction

The worldwide rapid expansion of obesity demands new noninvasive treatment strategies, which may be obtained via dietary interventions that suppress appetite sensations and regulate food intake [1,2]. Among others, oral and gastrointestinal (GI) processes involved in food intake regulation, and nutrient sensing in the small intestine can induce negative feedback signals to the proximal GI tract and central nervous system to inhibit digestion, appetite sensations, and food intake [3,4]. The ileum is believed to provide the strongest signal, through "the ileal brake" [5,6]. Ileal brake activation has

Abbreviation: AUC, area under the curve; BMI, body mass index; GI, gastrointestinal; SEM, standard error of the mean; VAS, visual analog scale; WPI, whey protein isolate.

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been proven via direct intraileal infusion of macronutrients, applying nasointestinal feeding catheters in human volunteers [6]. Already 30 years ago, ileal infusion of lipids was shown to reduce food intake [7,8]; however, as part of a long-term weight management strategy, ileal lipid delivery needs to be achieved via oral ingestion, so without need for intubation.

The degradation products of lipid digestion (ie, free fatty acids, monoglycerides) activate the ileal brake more than the intact lipids itself [1,9,10], but to achieve this lipid degradation, products need to be delivered to the ileum without proximal absorption. Under physiological conditions, orally ingested lipids are not likely to deliver discernible amounts of such degradation products to the ileum due to a range of processes that allow efficient lipolysis and absorption in the proximal small intestine [11]. To enable delivery of the lipolysis products, lipids need to be protected by a carrier that remains intact under the acidic conditions in the stomach and that slowly releases degradation products in the distal small intestine [1].

Many attempts have been made to control in vitro lipid digestion, mainly through designing a protective interface structure around nanometer- or micrometer-sized emulsion droplets [12]. However, such strategies are not effective enough to deliver lipolysis products to the distal small intestine even when sophisticated particle-stabilized interfaces [13,14] or multilayered interfaces [15,16] are used. This has led us to conclude that to truly control lipolysis, a different approach is needed that focuses on controlling the exposure of the lipids to digestive enzymes in the GI tract by incorporating lipids in a gel [17]. Oil-in-water emulsions encapsulated in calcium-alginate beads (named *emulsion-alginate beads* from hereon) have been suggested for this purpose, as the indigestibility of alginate preserves the structure of the beads, and the pH-dependent response favors lipase diffusion toward encapsulated emulsified lipids in the small intestine; namely, the beads shrink under acidic conditions and have a smaller mesh size, thereby protecting the encapsulated emulsion in the stomach. At increasing pH, such as in the small intestine, the beads swell and increase in mesh size [18-22]. This makes the oil droplets more accessible for lipase, but lipase diffusion in the beads is still considerably lower compared to free diffusion.

Emulsion-alginate beads have been shown to improve the integrity of the encapsulated lipids (as observed by microscopy) during gastric transit and to delay intestinal lipid absorption compared to free emulsion droplets or emulsion microclusters in rats [23]. These findings were in line with a human trial in which large (0.5 cm) lipid-core alginate-shell capsules were shown to delay intestinal lipolysis and absorption [24]. For the current human intervention study, small alginate beads (d_{32} = 0.5-1.2 mm) that encapsulate emulsion droplets (d_{32} ~25 μm; safflower oil as appetite suppressor [25]) were developed to delay intestinal lipolysis. In earlier work, it was shown that these beads can be designed to control in vitro lipolysis after prior gastric incubation by altering bead and mesh size [22]. Monitoring dynamic in vitro lipolysis of such emulsion-alginate beads confirmed lipolysis at time scales relevant for delivery to the more distal part of the small intestine, whereas in vitro lipolysis of nonencapsulated emulsions was almost completed when leaving the duodenal compartment [26].

The hypothesis for this study was that delayed release of encapsulated lipids suppresses appetite sensations and reduces food intake. The primary objective was to investigate the efficacy of encapsulated emulsions in calcium-alginate beads at reducing food intake during ad libitum meal consumption. The second objective was to investigate the efficacy of these beads at suppressing appetite sensations. The emulsion-alginate beads were ingested in a yogurt (active) and compared to a yogurt with an equienergetic mixture of nonencapsulated nutrients with comparable sensory properties (control) in a randomized placebo-controlled trial with crossover design. The present work is an explorative study to prove the concept of ileal brake activation in healthy overweight individuals.

2. Methods and materials

2.1. *Materials*

Safflower oil was purchased from De Wit Specialty oils (19200 Safflower Oil High Linoleic Refined; de Waal, the Netherlands), whey protein isolate (WPI) from Davisco Foods International (BiPro, purity 97.5%; Eden Prairie, MN, USA), calcium chloride from Boom BV (Prills Food grade; Meppel, the Netherlands), and sodium alginate (W201502) from Sigma Aldrich (St Louis, MO, USA). Fat-free yogurt, bread, marmalade, lemon juice, and the pasta meals were purchased at a local supermarket. All materials were certified for food-grade use and used directly without further purification.

2.2. *Preparation of the enriched yogurts*

Commercial fat-free yogurt (Campina Magere yogurt; Amersfoort, the Netherlands; energy density per 100 g: 39 kcal (163 kJ), 0 g lipid, 4 g carbohydrates, 4.7 g protein) was enriched with emulsified safflower oil (6 g) being either encapsulated in alginate beads (active) or nonencapsulated (control; in presence of "empty" beads), as schematically shown in Fig. 1.

2.2.1. *Emulsion*

Safflower oil was added to a WPI solution (20 wt% oil, 10 g·L^{-1} WPI in the aqueous phase) and mixed using a rotor stator homogenizer (Ika T18 basic Ultra-Turrax homogenizer equipped with a S18N-19G dispersion tool, Staufen, Germany) for 5 minutes at 13 000 rpm to obtain an emulsion with a droplet size (d_{32}) of 25 μm.

2.2.2. *Emulsion-alginate beads*

Fresh emulsion (<5 minutes after production) was mixed with an alginate solution (36 g·L^{-1}) in volume ratio 1:1 (final composition: 10 wt% oil, 20 g·L^{-1} alginate in the aqueous phase, Table 1). This alginate-emulsion mixture was added dropwise to a gently stirred calcium bath (5 wt% $CaCl_2$ with some drops of lemon juice to lower the pH and fully dissolve the calcium), as described previously [22]. The needle tip (inner diameter 0.41 mm; Nordson EFD, Dunstable, UK) was positioned 5-6 cm above the calcium bath, and a syringe pump was used to regulate the flow rate (3.0 mL/min). To control the bead size, an air flow was applied (Jun-Air 86R-4B compressor, Benton Harbor, MI, USA) such that it passed the needle in a homogeneous way, resulting in a bead size (d_{32}) of 1.10 ± 0.05 mm. After production, the emulsion-alginate beads were stored at 4°C at least overnight to harden completely

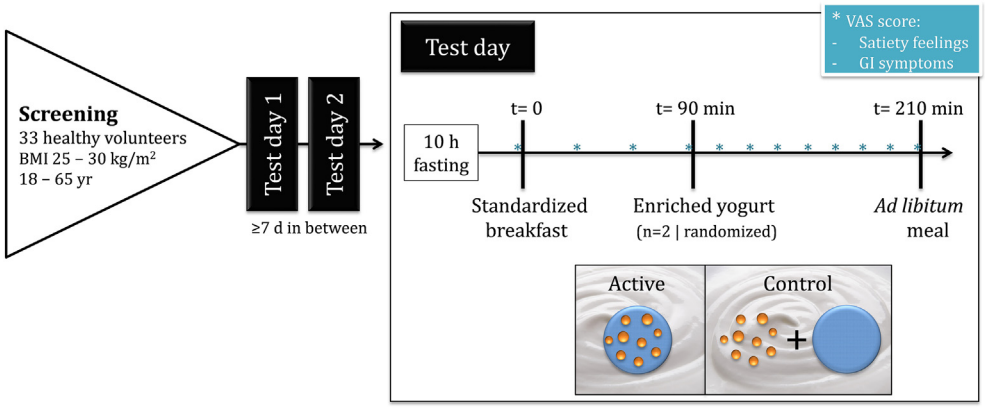

Fig. 1 – Overview of the study design on the effect of encapsulation of lipids on appetite sensations and food intake. Yogurts were enriched with 2 types of lipid carrier: either encapsulated as emulsion-alginate beads for ileal delivery (active) or nonencapsulated with comparable sensory properties (control). *VASs were used for 9 attributes per time point.

and not more than 4 days to prevent microbial spoilage. On the test day, the beads were filtered and washed with tap water (10 times volume, >10 minutes) and filtered again to obtain weighable beads.

2.2.3. *Empty beads*

Alginate beads were produced from 20 g·L^{-1} alginate solution in the same way as described above [22] but not mixed with emulsion. The bead size was 1.21 ± 0.02 mm, so it was similar to the emulsion-alginate beads. These beads were also stored at 4°C for 1 to 4 days and washed and filtered before use.

2.2.4. *Active yogurt*

Fat-free yogurt (120 g) was mixed with 60 g emulsion-alginate beads (containing 6 g safflower oil). The composition was matched to the control yogurt by adding 24 g water. The active yogurts contained 105 kcal (439 kJ), of which 51 kcal% came from the encapsulated lipids (Table 1).

2.2.5. *Control yogurt*

Fat-free yogurt (120 g) was mixed with 30 g emulsion (containing 6 g safflower oil), and 54 g empty beads to match the composition and sensory properties of the active yogurt. This makes the control yogurt an equienergetic mixture of nonencapsulated nutrients that also contained 105 kcal (439 kJ), of which 51 kcal% came from the nonencapsulated lipids (Table 1).

Table 1 – Composition and energy content of the studied yogurts

Name	Active (g)	Control (g)
Safflower oil	6.0	6.0
Whey protein	≤0.24	0.24
Alginate	1.08	1.08
Water[a]	76.9	76.9
Yogurt	120	120
Total	204	204
Total	105 kcal (439 kJ)	105 kcal (439 kJ)
Contribution of lipids	51 kcal%	51 kcal%

[a] Sum of the water added (in emulsion) and the water in beads.

2.2.6. *Particle size distribution*

The particle size distribution of the emulsions and beads was determined using static light scattering (Mastersizer 2000 with Hydro SM dispersion unit, Malvern Instruments, UK). For the emulsions, the refractive index of safflower oil was set at 1.460 and that of the dispersant at 1.333. For the beads, the refractive index was set at 1.470 (with an absorption index of 0.02) and the refractive index of the dispersant at 1.333.

2.3. *Study population*

The study population included 33 healthy overweight volunteers (male and female, 18-65 years, body mass index [BMI] 25-30 kg/m^2). Participants received 75 euro after completing the study. Thirty-one subjects were needed to complete the study based on an a priori power analysis for expected effect on our primary outcome, ie, food intake, so 33 subjects were included to account for possible dropouts. The expected effect size was based on differences in reduction of energy intake of the next meal from previous [4,5] and unpublished work: average difference of 82 kcal (343 kJ) with an average SD of 156 kcal (653 kJ).

The volunteers were recruited from a pool of subjects and via advertisements. Subjects were excluded from participation when they reported milk (protein or lactose) allergy/intolerance, dieting, pregnancy, lactation, excessive alcohol consumption (>20 U per week), intention to stop smoking, self-admitted HIV-positive state, abnormal eating behavior, or unexplained weight loss/gain in the month prior to screening. Subjects were also excluded when taking medication that may affect appetite and sensory function or who reported metabolic or endocrine disease, GI disorders, or a history of medical or surgical events that may have affected study outcome. All included subjects (n = 33; mean age: 43 years; mean BMI: 27.7 kg/m^2; 14 male) completed the protocol.

2.4. *Study design*

In this randomized, single-blind, placebo-controlled trial, the effect of 2 enriched yogurts was compared in a crossover design and focused on food intake and appetite sensations. The yogurts differed in the carrier of the lipid: either

encapsulated inside alginate beads for ileal delivery (active) or nonencapsulated with comparable sensory properties (control). For an overview of the study design, see Fig. 1.

2.5. Protocol

Every subject received 2 treatments on 2 different days with at least 1 week of washout period, following a randomized crossover design. On each test day, the subject arrived after a 10-hour fast at the Metabolic Research Unit at the Maastricht University Medical Center+. Per test day, 1 to 4 subjects were present simultaneously and were allowed to bring a book or laptop, but they could not see each other during meal intake. First, compliance to the previously mentioned rules was checked, and baseline measurements were done for appetite sensations and GI symptoms. The experiment started with intake of a standardized small breakfast (bread with marmalade; overall composition per 100 g breakfast: 235 kcal (983 kJ), 0.8 g fat, 6.8 g protein, 48 g carbohydrate, 3.5 g fiber; with 150 mL water or tea; t = 0 minute) that was identical on both test days. This small breakfast was provided because ileal brake feedback is less pronounced after a prolonged fasting state. When all or most of the breakfast was expected to have been emptied from the stomach (t = 90 minutes), the subject received 1 of the 2 yogurts (active or control) with 150 mL water or tea. Visual analog scale (VAS) scores for appetite sensations and GI symptoms were collected at a 30-minute interval before ingestion of the yogurt and a 15-minute interval after ingestion. Ad libitum food intake was assessed 2 hours after intake of the test yogurts, as this reflects the anticipated application of an ileal brake–inducing food product, which targets to decrease energy intake during a subsequent meal. Food intake was calculated (kcal) from the difference in weight of the plate before and after ad libitum food intake of a large pasta meal (>1 kg; Lasagna Bolognese, PLUS Supermarket; Utrecht, the Netherlands; energy density per 100 g: 152 kcal (636 kJ), 8.6 g lipid, 11.0 g carbohydrates, 7.1 g protein). After meal consumption, the test day finished.

2.5.1. Appetite sensations and GI symptoms

VAS scores [27,28] were used to determine appetite sensations (satiety, fullness, hunger, desire to eat, desire to snack) and GI symptoms (bloating, discomfort, pain, nausea), in total at 12 time points (t = 0, 30, 60, 90, 105, 120, 135, 150, 165, 180, 195, and 210 minutes) per test day. All attributes were measured using a VAS from 0 to 100 mm, with the most negative or lowest-intensity feelings at the low end and the opposing terms at the high end. The subjects indicated their feeling at that moment; scoring forms were collected immediately to prevent use as reference for later scorings.

2.6. Ethics

The study was approved by the Medical Ethics Committee of the Maastricht University Medical Center+ and was conducted in full accordance with the principles of the Declaration of Helsinki of 1975 as amended in 2013 and with the Dutch Regulations on Medical Research involving Human Subjects (1998). All participants gave written informed consent before participation. This trial was registered at clinicaltrials.gov as NCT03025997 and was performed at the Maastricht University Medical Center+ from January until March 2017.

2.7. Statistical analyses

The SPSS statistical software package Version 23.0.0.2 (IBM SPSS Statistics, Chicago, IL, USA) was used for statistical analysis. Statistical significance was set at $P < .05$ in all tests. A descriptive analysis of the study population was performed first, including the independent variables age, sex, and BMI, and reported as means ± standard errors of the means (SEMs).

According to an a priori power analysis based on the expected effect size, 31 subjects needed to complete the study for a power of 80% and P value of 5% (2-sided significance level). The dependent variables were checked to meet homogeneity of variance, and normality was checked and tested (Shapiro-Wilk test). To compare food intake (kcal) after intake of the control and active yogurt, a paired-samples t test was performed (n = 33).

Because the raw VAS data did not meet the requirements of normality, we tested the difference between control and active yogurt (n = 33) through area under the VAS curves from ingestion of the yogurt (t = 90 minutes) until ad libitum meal consumption (t = 210 minutes). Total areas under the curve of VAS scores were calculated using the trapezoid rule [27] and did meet normality (Shapiro-Wilk test) for satiety, fullness, hunger, and desire to eat. Therefore, the effect of yogurt on these area under the curve (AUC) VAS scores was tested with paired-samples t tests (n = 33), with Bonferroni correction for multiple comparisons to eliminate type I errors. For GI symptoms, scores were all very low, and the difference in AUC VAS did not meet normality (Shapiro-Wilk test), so nonparametric tests for related samples (Wilcoxon signed ranks test, n = 33) were performed. All data are reported as means ± SEM in the "Results" section.

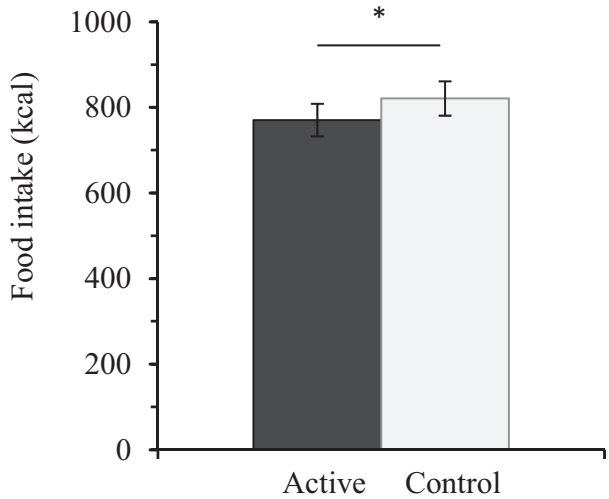

Fig. 2 – Food intake measured during ad libitum meal consumption 2 hours after ingestion of the active yogurt (black bar) or control yogurt (light bar).Values are means ± SEM. The difference is significant in a paired-samples t test (*P ≤ .05, n = 33).

3. Results

3.1. *Food intake*

The primary goal of the study was to assess the efficacy of emulsion-alginate beads to reduce food intake through activation of the ileal brake. Fig. 2 shows the food intake during ad libitum meal consumption 2 hours after ingestion of the active yogurt (black bar; 770 ± 38 kcal (3222± 159 kJ)) or control yogurt (light bar; 821 ± 40 kcal (3435 ±167 kJ)). After ingestion of the active yogurt, food intake was significantly lower (51 ± 20 kcal (213 ±84 kJ); P = .016) compared to the control, which accounts for a reduction of 6.2% in energy intake.

3.2. *Appetite sensations*

The efficacy of the test product to suppress appetite (increased feelings of satiety and fullness; reduced feelings of hunger, desire to eat, and desire to snack) was determined as secondary study parameter by comparing VAS scores. Fig. 3 shows comparable VAS scores for appetite sensations after ingestion

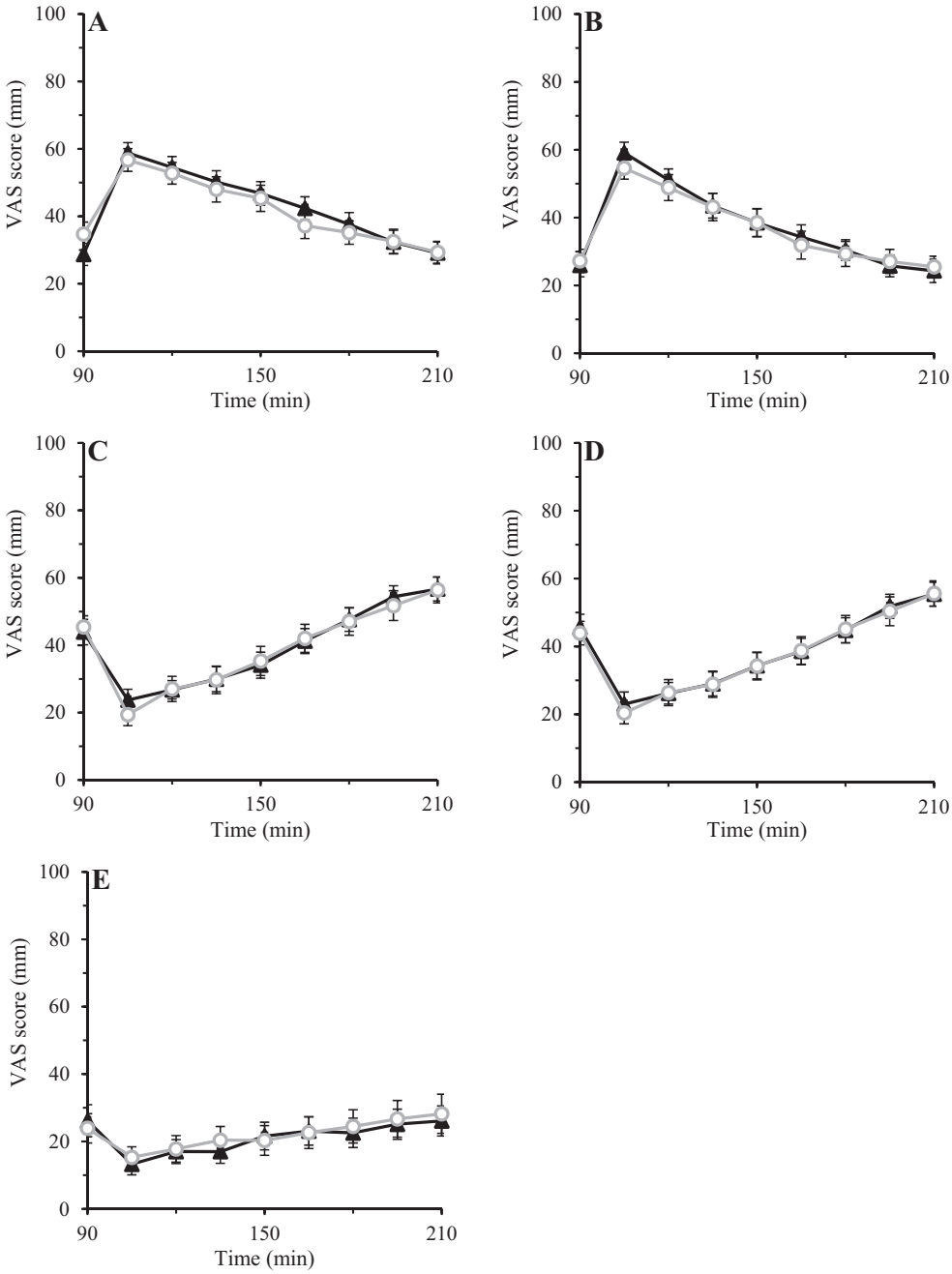

Fig. 3 – VAS scores for satiety (A), fullness (B), hunger (C), desire to eat (D), and desire to snack (E) after ingestion of the active yogurt (filled symbols) and control yogurt (open symbols), measured on a 100-mm scale. The yogurt was ingested at t = 90 minutes (90 minutes after breakfast) and ad libitum meal was consumed at t = 210 minutes.Values are means ± SEM (n = 33).

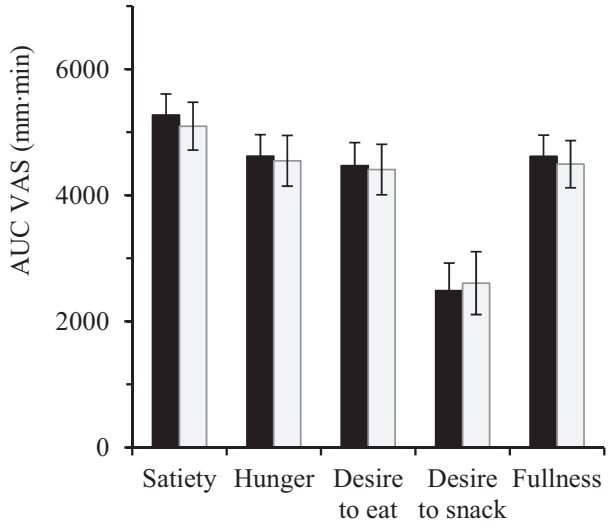

Fig. 4 – Total AUCs of VAS scores for appetite sensations from ingestion of the active (black bar) or control (light bar) yogurt (t = 90 minutes) until ad libitum meal consumption (t = 210 minutes).Values are means ± SEM. No significant differences (n = 33, paired-samples t tests).

of the active yogurt (filled symbols) and control yogurt (open symbols).

None of the attributes differed significantly in AUC VAS scores when comparing active and control (Fig. 4; AUC VAS for satiety, $P = .5$; for hunger, $P = .8$; for desire to eat, $P = .8$; for desire to snack, $P = .6$; for fullness, $P = .7$).

3.3. *GI symptoms*

Fig. 5 shows that all measured GI symptoms were low (<10 mm, measured on a 100-mm scale) and none of the attributes differed significantly in AUC VAS scores between active and control (Wilcoxon signed ranks test, n = 33; bloating, $P = .9$; discomfort, $P = .5$; pain, $P = .5$; nausea, $P = .4$). Evaluation of adverse events only showed 3 subjects with short-term diarrhea: 2 on the day of the control yogurt and 1 on the day after the active yogurt.

3.4. *Subject expectation of ingested intervention*

After finishing the second test day, subjects were asked to indicate on which test day(s) they thought to have consumed the active and control yogurt; 15 subjects indicated correctly the

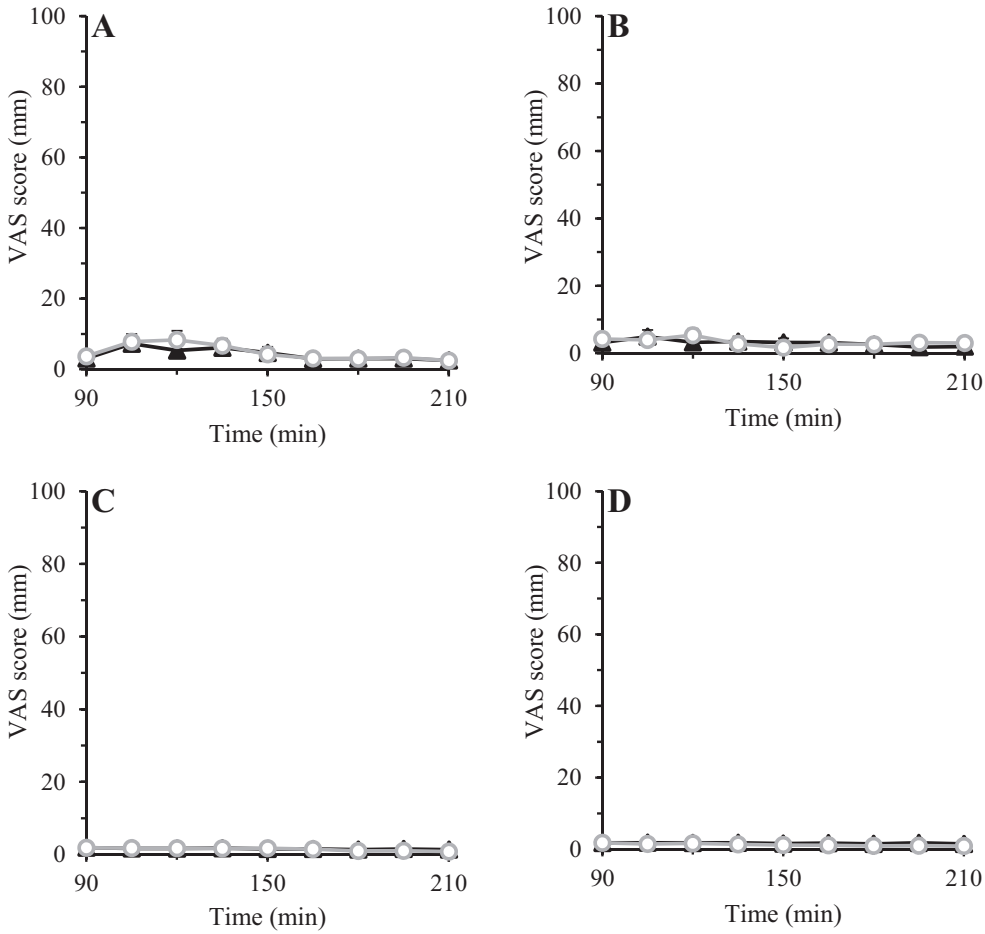

Fig. 5 – VAS scores for bloating (A), discomfort (B), pain (C), and nausea (D) after ingestion of the active yogurt (filled symbols) and control yogurt (open symbols), measured on a 100-mm scale. The yogurt was ingested at t = 90 minutes (90 minutes after breakfast), and ad libitum meal was consumed at t = 210 minutes.Values are means ± SEM (n = 33).

test day on which they consumed the control yogurt (feeling hungrier), and 7 subjects indicated the wrong intervention; 11 subjects indicated to have perceived no difference in hunger feelings between the 2 days.

4. Discussion

We have shown that ingestion of a yogurt containing emulsion-alginate beads results in a small but statistically significant reduction in food intake during a subsequent meal (–6.2% energy intake) compared to the control yogurt that contained an equienergetic mixture of nonencapsulated nutrients with comparable sensory properties. We therefore accept the hypothesis that delayed release of encapsulated lipids reduces food intake. When extrapolating our findings directly to a daily basis, a reduction of 155 kcal (649 kJ) could be achieved for a 2500-kcal (10460 kJ) intake. This is considered to be a relevant reduction, as a daily reduction of 50 kcal (209 kJ) could already prevent weight gain in about 90% of the population [29].

To the best of our knowledge, this is the first human intervention study exploring the effects of emulsion encapsulation in calcium-alginate beads on food intake and appetite sensations. In other studies, lipid-core alginate-shell capsules have been shown to control the gastrointestinal fate of lipids and to slightly increase satiety scores [24], but in the present work, we use smaller lipid droplets and therefore smaller beads.

None of the appetite attributes differed significantly between active and control (satiety, fullness, hunger, desire to eat, and desire to snack). Thus, although emulsion-alginate beads clearly affect eating behavior, no relevant change in appetite sensations was observed.

Reduced food intake through activation of the ileal brake has previously been proven with direct intraileal infusion of lipids [4,5,7] but not after oral ingestion. Up until now, the most promising emulsion system to deliver degradation products of lipid digestion in the distal small intestine was an emulsion of palm oil and oat oil fractions that naturally contain galactolipids, which was commercialized as Fabuless, Olibra, and Reducal. The galactolipids were expected to induce nucleation and growth of saturated fatty acids crystals, which are absorbed more slowly from the intestine [30] and were claimed to improve weight management [31]. However, Fabuless loses its functionality during normal food-manufacturing processes (thermal and shear processing) [32]. Compared to intubation studies that deliver exact amounts of lipids directly to the target position [6], the effect that we find here is less pronounced. This may be related to less optimal timing and dosages of the release of lipids. Secondly, lean subjects were used in the intubation studies, whereas we studied overweight subjects, who are known to be less sensitive for intraluminal lipids [33].

We also anticipated that part of the encapsulated lipids will have remained unabsorbed. Ad libitum food intake was assessed 2 hours after intake of the test yogurts, as this reflects the anticipated application of an ileal brake–inducing food product, which targets to decrease energy intake during a subsequent meal. Within this time scale, we observed no significant effect of the yogurt type on scores of appetite sensations. Based on the average gastric emptying profile of yogurt, about half of the emulsion-alginate beads was expected to reach the small intestine within 45 minutes after ingestion [34], and once in the small intestine, half of the lipid digestion products was expected to be released within 2.5 hours based on previous observations in a static in vitro model [22]. Based on the in vitro observations, it is likely that only a part of the encapsulated lipids will have been digested before subsequent meal consumption started. This may explain why both interventions did not show differences in appetite sensations.

Further optimization of the emulsion-alginate beads is still possible to increase practical significance for the treatment of obesity. To tailor the release of lipids, not only the size of the beads and/or the mesh size can be considered as described previously for in vitro studies [22], but also the emulsion droplet size can be used to greatly influence lipolysis by changing the available interfacial area [35-37]. Increasing the amount of lipids per bead volume is not considered an option because this decreases density and will result in floating of the beads in the stomach [38] and, thus, delays emptying of the active components into the small intestine.

The control yogurt is considered an appropriate reference for the active yogurt, as the free emulsion is rapidly digested and the lipid metabolites will probably be absorbed completely before reaching the distal small intestine [1,9,10]. Moreover, the empty beads can be conveniently used to design equienergetic products that have no difference in mouth feel, as none of the subjects indicated a difference in sensory properties between the 2 yogurts.

A limitation of the present study is that the distal release of lipids from the used encapsulates was not tested during the in vivo experiment, but instead, the digestion dynamics of the encapsulated lipids were anticipated based on in vitro observations. Additional mechanistic studies would be the next step to take, which includes measuring delivery of lipids from ingested emulsion-alginate beads in vivo in the intestinal lumen. Besides, although we took the best possible care, it is always possible that, in single-blind design, the researcher may (un)intentionally have given subconscious cues which influence the subjects. A third limitation of the present study is the rather short period of controlled behavior prior to starting the test day in the research facility (10-hour fast). This might have been too short to minimize influences from the day before on the test day, such as within-person variation in eating behavior and physical exercise. The crossover study design minimized the influence of between-person variations.

Before this product can be used in weight management applications, additional studies will need to be conducted. The duration and impact of the single-dose effect will have to be determined, with concomitant assessment of biological markers (ie, gut hormones as PYY and GLP-1) to gain insight in the involved satiating mechanisms. In a next phase, the effects of this product concept on body weight regulation will have to be investigated in long-term intervention studies, while also charting possible habituation and compensation.

The future perspectives of emulsion-alginate beads for noninvasive weight management are promising because these

beads can be incorporated into a yogurt-like food product that is part of a normal diet. It is also good to mention that there are positive developments in production technology to produce similar emulsions and beads at a large scale [39].

In conclusion, we demonstrated that ingested emulsion-alginate beads significantly decreased food intake in overweight individuals compared to an equienergetic mixture of nonencapsulated nutrients with comparable sensory properties. We hypothesize that this reduction in food intake is caused by delayed release of encapsulated lipids in the distal small intestine, which activates the ileal brake mechanism. To gain further understanding of ileal brake activation via dietary routes for weight management, additional studies on dose-response relations and long-term effectiveness need to be conducted. If successful, this strategy could result in noninvasive methods for weight control.

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