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Published in:
Metabolism - Clinical and Experimental

DOI:
10.1016/j.metabol.2019.154043

Published: 31/03/2020

Document Version
Peer reviewed version

Link to publication on the UWS Academic Portal

Citation for published version (APA):

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Moderate intensity exercise training combined with inulin-propionate ester supplementation increases whole body resting fat oxidation and reduces adiposity in overweight women

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Word Count: 1483
ABSTRACT

Background: Our previous work has shown that oral supplementation with inulin propionate ester (IPE) reduces intra-abdominal fat and prevents weight gain and that oral propionate intake enhances resting fat oxidation. The effects of IPE combined with exercise training on energy substrate utilisation are unknown. The aim of this study was to investigate the impact of 4-weeks IPE supplementation, in combination with a moderate intensity exercise training programme, on whole body fat oxidation and on plasma GLP-1 and PYY.

Methods: Twenty overweight healthy women participated in randomised parallel study and underwent 4 weeks of supervised exercise training either with IPE (EX/IPE group) or Placebo (EX/Placebo group) supplementation. Before and after the intervention participants conducted an experimental trial, which involved collection of expired gas and blood samples in the fasted state and during 7 hours of the postprandial state.

Results: Within groups, the EX/IPE group significantly enhanced the amount of fat (Pre, 24.1 ± 1.2 g; Post, 35.9 ± 4.0 g, P< 0.05) oxidised and reduced CHO (Pre,77.8 ± 6.0 g; Post, 57.8 ± 7.7 g, P< 0.05) oxidised, reduced body weight (Pre, 77.3 ± 4.2 kg; Post, 76.6 ± 4.1 kg, P< 0.05) and body fat mass (Pre, 37.7 ± 1.9 %; Post, 36.9 ± 1.9 %, P< 0.05). In EX/Placebo group, changes in amount of fat (Pre, 36.8 ± 3.9 g; Post, 37.0 ± 4.0 g) and CHO (Pre, 62.7 ± 6.5g; Post, 61.5 ±7.4 g) oxidized, body weight (Pre, 84.2 ± 4.3 kg; Post, 83.6 ± 4.3 kg) and body fat mass (Pre, 40.1 ± 1.9 %; Post, 38.7 ± 1.5 %) were not significant. Comparing between groups, change in the amount of fat oxidised was significantly (P<0.05) higher for EX/IPE compared with EX/Placebo and there was a trend for difference for amount of CHO oxidised (P=0.06) and RER (P=0.06). Energy expended was not significantly different (P>0.05). The interventions had no impact on fasting or postprandial plasma concentrations of GLP-1 and PYY.
Conclusion: Moderate intensity exercise training programmes when combined with daily oral IPE supplementation may help overweight women to achieve increase in fat oxidation.

The study was registered at clinicaltrials.gov as NCT04016350.

Key words: Exercise, inulin propionate ester, fat oxidation, gut hormones, body weight
1. Introduction

Increasing exercise is important in obesity reduction strategies, inducing negative energy balance driven by increasing energy expenditure [1]. However, the effectiveness of exercise induced weight loss in the absence of caloric restriction remains controversial and is highly individual [2-5]. In healthy overweight women, who participated in 7 week-endurance-type exercise programme and achieved variable changes in fat mass and fat oxidation, energy expenditure and the change in resting fat oxidation were the only statistically significant independent predictors of change in fat mass [6]. This suggests that strategies maximizing resting fat oxidation may enhance body fat mass loss alongside exercise in overweight and obese individuals.

The short chain fatty acid (SCFA) propionate, produced through fermentation of dietary fibre by the gut microbiota, has a range of metabolic benefits [7]. Previous work has reported that that a single dose of oral sodium propionate increased both resting energy expenditure and resting fat oxidation in humans [8]. These findings are in line with a recent report that rectal SCFA infusion, high in propionate, increases resting energy expenditure and fat oxidation in overweight men [9]. Together, these data suggest that increasing propionate production in the gut may be useful in an overall weight management strategy. We developed inulin propionate ester (IPE) to target delivery of propionate to the colon, mimicking high-fibre dietary intake using a modest supplement dose [10].

Thus, the main aim of this study was to investigate the impact of daily IPE supplementation combined with 4-week exercise training programme on whole-body fat oxidation and body fat change in overweight women. Since our previous study [10] reported that acute ingestion of 10 g IPE significantly increased postprandial plasma PYY and GLP-1, and that this effect on the incretin response was lost following long-term (24-week) supplementation, this study also investigated the postprandial anorexigenic gut hormones response.
2. Participants and Methods

This single blinded randomised parallel study was conducted on healthy overweight females with BMI >25 kg/m² and 25-45 years of age. Study participants underwent 4 week supervised moderate intensity exercise training combined either with IPE (EX/IPE) or cellulose as placebo (EX/Placebo) supplementation. Before and at the end of the 4-week intervention, participants underwent body weight and body composition measurements, conducted a submaximal exercise test and a 7-hour experimental trial, which involved collection of expired air and blood samples in fasted and postprandial states. Detailed description of the participants, study design and methods are available in the online-only Supplementary Material.

3. Results

3.1. Changes in body weight and body fatness

Physical characteristics of the participants measured before and after 4-week interventions are presented in Supplementary Table 1. Participants of the EX/Placebo group (n=11) exercised at a HR of 146 ± 4 beat·min⁻¹, which corresponded to 61 ± 1 % of the predicted maximal oxygen consumption and the participants of the EX/IPE (n=9) group exercised at a HR of 142 ± 5 beat·min⁻¹, which corresponded to 60 ± 2% of the predicted maximal oxygen consumption. The total energy expenditure of the exercise programmes was not significantly different between groups (EX/Placebo, 5768 ± 412; EX/IPE, 5469 ± 390 kcal) and body weight loss of 0.77 ± 0.16 kg and 0.74 ± 0.17 kg was expected in EX/Placebo and EX/IPE groups, respectively. In the EX/Placebo group, the 4-week exercise programme had no effect (P>0.05) on mean body weight, BMI, body fat mass and body fat percentage whereas in the EX/IPE group post-intervention body weight, BMI, body fat mass and body fat percentage were significantly (P<0.05) lower in comparison to the pre-intervention values. The differences...
between body weight and body fat changes in EX/Placebo and EX/IPE groups were not significant but in the EX/IPE group responses were less variable.

### 3.2. Fat and CHO oxidation during 7-hour trials

In EX/Placebo group, four weeks of intervention had no significant impact on fat and CHO oxidation rates while in the EX/IPE group difference in pre- and post-intervention rate of fat oxidation was significant ($P<0.05$, two-way ANOVA, trial effect) (Figure 1). In the EX/Placebo group, the intervention had no impact on total amount of fat and CHO oxidised while in the EX/IPE group intervention increased the amount of fat ($P<0.05$) and reduced the amount of CHO ($P<0.05$) oxidised (Table 1). Comparing between groups, changes in the amount of fat oxidised were significantly ($P<0.05$) different and a trend for difference was observed for amount of CHO oxidised ($P=0.06$) and RER ($P=0.06$). Energy expended was not significantly different ($P>0.05$) (Table 1).

### 3.3 Appetite-related gut hormones

In both, the EX/Placebo and EX/IPE groups, four weeks of intervention had no significant effect on plasma concentrations of plasma GLP-1 and PYY ($P>0.05$, two-way ANOVA, trial effects). Comparing between groups, changes in time-averaged areas under the responses of PYY or GLP-1 versus time curves were not statistically different (Supplementary Table 2). In EX/IPE group, time averaged areas under the curve of GLP-1 measured during both, pre-intervention and post-intervention trials, were significantly ($P<0.05$, unpaired t-test) higher than in EX/Placebo group while pre-intervention and post-intervention concentrations of PYY were not different between EX/IPE and Ex/Placebo groups (Supplementary Table 2).

### 4. Discussion

This first-in-human study demonstrates that IPE supplementation leads to increased resting whole-body fat oxidation in the postprandial state when combined with moderate intensity 4-
week exercise programme in overweight women. We found that the change in the amount of
fat oxidised during seven hours of the experimental trial was significantly higher in the IPE
than Placebo group and the difference in the change in fat oxidations between groups
consisted of approximately 10 grams. Thus, the beneficial effects observed on fat oxidation
with single dose propionate oral consumption [8] translate into other physiological states,
including during exercise training. As in some other studies [11,12] resting fat oxidation was
not affected by four weeks exercise training combined with placebo. Thus, enhanced fat
oxidation seen in IPE group most likely relates to daily intake of IPE rather than to
participation in the exercise programme. We note that fat oxidation measurements were
conducted at least 18 hours after intake of the last IPE dose. Thus, supplementation with IPE
had a long-term rather than acute effect on resting fat oxidation.

As in majority of exercise training studies without dietary restriction [13], predicted
body weight loss was modest and not clinically significant (≤5% weight loss). In the control
group intervention had no significant effect on mean body weight and body fatness and as in
other studies [4-6, 14] the responsiveness to exercise training was also variable. The IPE
group achieved a significant reduction in body weight and body fatness and changes were
less variable than in the control group. Taking into consideration that in the control group,
changes in fat oxidation were found only in some participants and that in IPE group fat
oxidation was enhanced in all participants, our data support the hypothesis that increase in fat
oxidation during exercise programmes is important for achieving improvements in body
weight and body fat. Further work is required to assess if the effects on body mass and
composition over longer duration persist with IPE in well-designed randomised controlled
trials.

We also found that IPE supplementation during exercise programme had no impact on plasma
concentrations of GLP-1 and PYY. This observation is novel and important and suggests that
GLP-1 and PYY response to IPE is attenuated within 4 weeks and thus persists much shorter than we previously reported in a 24-week intervention study [10]. However, as with fat oxidation measurements, collection of blood for hormone measurements occurred 18-24 hours after intake of the last IPE dose and thus acute elevation GLP-1 and PYY after IPE cannot be ruled out. The finding that concentrations of GLP-1 and PYY were not modified by exercise intervention alone is consistent with findings from other similar studies [5,15].

This study has limitations. Data obtained in this study do not allow to establish causality between IPE induced change in fat oxidation and change in body fatness. This should be investigated by future studies which include measurements of behavioural compensatory variables such as changes in energy intake and energy expenditure of physical activity outside exercise sessions, known to contribute to the responsiveness to exercise training programmes [16-18]. It is possible that increasing the number of participants could lead to significant changes in GLP-1 and PYY concentrations in IPE group and differences between post- and pre-intervention CHO oxidation were seen at additional time points. We note that this was a preliminary study and we had no way to formally calculate a sample size for study outcomes. Thus, with the data from the present study, further appropriately powered, randomised controlled trials to investigate the longer-term effects of IPE on body weight in both men and women alongside prescribed exercise interventions are warranted. Considering appetite regulating hormones beyond GLP-1 and PYY [19] will also be important in future studies.

In conclusion, this study demonstrates that adding IPE to moderate intensity exercise programmes, applied to overweight women, achieves an increase in whole-body resting fat oxidation.

Author contributions
DJM, DM, KG, ESC, CMT, GF contributed to the concept development and designed study; TP, ER recruited participants and conducted the experimental work; ER, DM performed appetite hormone analysis and statistical analyses; DJM, DM drafted the manuscript; All authors contributed to revisions of the manuscript. None of the authors had a personal or financial conflict of interest to disclose.

**Funding**

This work was supported by the Biotechnology and Biological Sciences Research Council (BBSRC; Grant No. BB/L004259/1).

**Disclosure Summary**

GF, DJM and TP are named inventors on the patent WO2014020344A1.

**Competing Interests**

None of declare.

**Acknowledgements**

We thank all participants who participated in this study and the administration of University of Glasgow Sports and Recreation Service for facilitating participants’ use of sports facilities for the exercise intervention.

**References**


training and weight loss, not always a happy marriage: single blind exercise trials in females with diverse BMI. Appl Physiol Nutr Metab 2018;43:363-70.


17. Silva AM, Júdice PB, Carraça EV, King N, Teixeira PJ, Sardinha LB. What is the effect of diet and/or exercise interventions on behavioural compensation in non-


**Figure Legends**

Figure 1. Rate of fat and carbohydrate (CHO) oxidation, and energy expenditure (EE) in the fasted state (0h) and during post-breakfast (0-180min) and post-lunch (180-420 min), measured before (Week 0) and after 4-week exercise intervention (Week 4) combined with Placebo (Ex/Placebo group, n=11) and Inulin Propionate Ester (Ex/IPE group, n = 9) supplementation. Values are means ± SEs.*Significant (P<0.05) difference at corresponding time points.