

Abstracts

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SA02

Continuous glucose monitoring systems and free-living glycaemic control in people with diabetes

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Glucose measurements are essential for diabetes management. Although the measurement of HbA_{1c} has been the traditional method for assessing glycaemic control, it does not reflect intra- or inter-day glycaemic excursions or identify periods of high or low blood glucose. Advancements in continuous glucose monitoring systems (CGMs) has enabled a greater insight into an individual's glycaemic control than what was once attainable by intermittent capillary blood sampling or from HbA_{1c}. CGMs track glucose concentrations in the body's interstitial fluid, providing near real-time glucose data over several days. Accordingly, there has been a push for additional CGM-derived glycaemic indices to be used to complement HbA_{1c} when assessing an individual's glycaemic control. This talk will cover the therapeutic use of CGMs in practice for people with diabetes and how they can also be used as a robust research tool.

SA03

Let's take it outside: non-invasive techniques to assess protein metabolism and anabolic sensitivity outside the lab

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Maintaining an adequate quantity and quality of lean tissue (including skeletal muscle) is important for health and performance across the lifespan. Lean tissues are constantly 'turning over' through the process of protein breakdown and synthesis with the algebraic difference determining net protein balance. Exercise and dietary amino acid ingestion are primary stimulators of synthesis whereas aging and/or inactivity may induce a relative 'anabolic resistance' as characterized by an attenuated utilization of dietary amino acids for tissue protein synthesis. Our foundational understanding of protein turnover in humans is based on the application of stable isotopes traditionally applied (e.g. intravenously infused) in controlled lab settings and involve invasive blood and tissue (e.g. muscle biopsy) sampling. However, development of techniques that can be used non-invasively and outside of traditional controlled laboratory settings are an advantage to the research and clinical communities given their ability to be deployed in remote settings and in vulnerable populations (e.g. children, older adults, clinical populations). We therefore adapted ¹³C-labeled amino acid methodologies to be utilized noninvasively and with minimal investigator oversight outside the lab to determine the 'anabolic sensitivity' of lean tissues and to define optimal daily protein requirements. These methods are based on the differential primary fate of dietary essential amino acids as substrates for: i) protein synthesis (i.e. retained in the body), or; ii) energy utilization (i.e. generating ¹³CO₂). Ingestion of 0.25g/kg of 'protein' (crystalline amino acids modeled on the composition of egg protein) enriched to 5% (~100mg) with [¹³C]leucine can detect exercise-induced anabolic sensitivity through a ~11% reduction (P<0.01) in ¹³CO₂ production (~10% greater leucine retention; P>0.01) after resistance exercise compared to non-exercise control (Mazzulla et al., 2022). Preliminary findings suggest this leucine 'breath test' can also detect 'anabolic resistance' of aging through a reduced leucine retention in older (~70y) compared to younger (~24y) men and women. To determine protein requirements remotely, we modified the indicator amino acid oxidation (IAAO) technique, which is based on the partitioning of [¹³C]phenylalanine between body protein synthesis and oxidation (OX), to be self-administered in male and female endurance athletes with only two suboptimal (0.2 and 1.2g/kg/d) and one excess (2.2g/kg/d) test protein intake. There was a difference (P>0.01) in OX between all test protein intakes with the modeled breakpoint indicating an estimated average requirement for protein of ~1.6g/kg/d and a safe intake (upper 95%CI) of ~1.8g/kg/d to maximize whole body protein synthesis during exercise recovery for both sexes. This recommended daily intake was identical to our previously determined requirement within a controlled lab setting using multiple test intakes (n=7 per participant), highlighting the utility of the IAAO to be adapted to remote research environments at a significantly lower participant burden. These noninvasive tracer methods have the potential for wide deployment (population and location) to advance our understanding of human protein turnover across the healthspan.

Mazzulla M. et al. (2022). Appl Physiol Nutr Metab 47, 860-870. Williamson E. et al. (2023). Med Sci Sports Exerc 55, 1866-75.

SA05

The application of stable isotope tracers to study muscle mass regulation in health and disease.

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Skeletal muscle is well known for its locomotory and key structural functions. In addition, skeletal muscle provides essential roles for maintenance of metabolic health, acting as a storage point for glucose, lipids, and providing the largest store of amino acids in the body. As such, maintenance of muscle mass is key to the promotion of health and well-being across the lifespan and in many disease states. Skeletal muscle loss, in either clinical, or non-clinical situations, is strongly associated with increased physical disability, reduced quality of life, and mortality. Significant attempts are being undertaken to prevent or delay the loss of muscle mass in both healthy individuals and in clinical settings. Nevertheless, the underlying regulation of muscle mass remains poorly characterized, resulting in a lack of effective therapeutics to tackle muscle wasting. Stable isotope tracers enable the study of dynamic muscle mass regulation, with the potential to provide novel insights into the mechanisms governing skeletal muscle loss and paving the way for the development of more focused therapeutic approaches. This talk will focus on the principles of stable isotopes tracers and how they can be applied to investigate muscle mass regulation in health and disease.

SA06

Brown and beige adipose tissue-derived metabokine inter-organ signalling in health and disease

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There is emerging evidence of a group of metabolites, which function to mediate cellular signalling and interorgan crosstalk, regulating local metabolism and systemic physiology. These bioactive metabolite signals have been termed metabokines. Brown and beige adipose tissue are understood to be distinct endocrine organs. These tissues are functionally associated with skeletal muscle, adipose tissue metabolism and systemic energy expenditure, suggesting an interorgan signaling network. Using metabolomics, we identify the metabolites 3-methyl-2-oxovaleric acid, 5-oxoproline, and β -hydroxyisobutyric acid as small molecule metabokines synthesized in browning adipocytes and secreted via monocarboxylate transporters. 3-methyl-2-oxovaleric acid, 5-oxoproline and β -hydroxyisobutyric acid induce a brown adipocyte-specific phenotype in white adipocytes and mitochondrial oxidative energy metabolism in skeletal myocytes both in vitro and in vivo. In rodent models of dietary-induced obesity BAT and beige adipose tissue thermogenic activity is blunted, with a reduction in the adipose tissue and circulating concentrations of the metabokines. In humans, plasma and adipose tissue 3-methyl-2-oxovaleric acid, 5-oxoproline and β -hydroxyisobutyric acid concentrations correlate with markers of adipose browning and inversely associate with body mass index. These metabolites reduce adiposity, increase energy expenditure and improve glucose and insulin homeostasis in mouse models of obesity and diabetes. Our findings identify beige adipose-brown adipose-muscle physiological metabokine crosstalk. The water solubility and oral availability of the metabokine signals suggest potential as dietary supplements to treat metabolic disease.

SA08

Nutrient Timing & Metabolic Regulation

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The physiological response to a given stimulus often depends on context. Specifically, the effects of certain variables involve interactions with other variables that do not all necessarily exert their influences at the same time. Many metabolic and behavioural parameters follow repeating patterns each day and this rhythmicity is linked to the temporal relationship between cycles in variables such as light exposure, sleep, activity and nutrition. This talk will introduce the broad concept of how circadian and diurnal rhythms can be either aligned or misaligned in this regard and consider how lifestyle patterns can therefore be linked to human health. After briefly considering recent studies that have characterised 24-h rhythmicity in human skeletal muscle during semi-constant routine protocols, we will then work systematically through a complete 24-h cycle, beginning with an examination of how the metabolic responses to an initial breakfast meal can exert carry-over effects to subsequent meals when using serial meal tests. We will then move through to the post-lunch period and consider the metabolic and behavioural effects of transitioning between the fed- and fasted-state at 1500 daily, within the context of an alternate-day model of intermittent fasting. Moving through to the evening, we will contrast overnight metabolic responses between individuals who have been fed continuously *versus* individuals who received bolus feedings at 0800 and 2000 h, before looking into the effects of nocturnal feeding (both throughout the night via enteral feeding during sleep and models involving waking up briefly in the early hours for a snack). Finally, we will complete the daily cycle by considering the metabolic responses to breakfast the morning after a night of fragmented sleep – and whether a strong coffee is a sensible remedy in that context.

SA09

The ins and outs of liver fat metabolism: effect of metabolic and nutritional state on the risk of metabolic disease

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The liver is a key metabolic organ that undertakes a multitude of physiological processes. It serves as an intermediary organ between exogenous (dietary) and endogenous energy supply to extrahepatic organs, with hepatocytes rapidly transitioning back and forth between the metabolic tasks of energy storage and supply. Given its pivotal role in regulating systemic lipid metabolism, perturbations in hepatic metabolism can impact on metabolic disease risk. For example, the accumulation of intra-hepatocellular triglyceride (IHTG), which likely results from an imbalance between fatty acid delivery to the liver, hepatic fatty acid synthesis and fatty acid removal (via oxidation or export as triglyceride (TG)) from the liver. Insulin is the main regulator of all these processes; insulin resistance has profound effects on liver fat metabolism. By using a combination of *in vivo*, *ex situ* and *in vitro* models with methodologies such as stable isotope tracers, there is the potential to gain insight into intra-hepatocellular lipid metabolism. This talk will review the insights gained from undertaking studies using these models of human liver metabolism and discuss how metabolic (e.g. adiposity) and nutritional state may alter hepatic fatty acid partitioning and influence the risk of metabolic diseases including insulin resistance, metabolic dysfunction-associated steatotic liver disease (MASLD) and cardiovascular disease.

SA12

The gut microbiota and sarcopenia

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The gut microbiota plays a crucial role in various metabolic processes such as carbohydrate fermentation, bile acid metabolism, and amino acid degradation. These processes generate metabolites and inflammatory signals that directly impact the metabolism of the host at peripheral organ sites, particularly skeletal muscle. Aging is associated with increased medication, reduced physical activity, and dietary modifications, all of which can alter the composition and metabolic activity of the gut microbiota. Consequently, the gut microbiota is implicated in several age-related diseases and conditions, including sarcopenia.

This presentation aims to provide an overview of the intricate relationship between aging and the gut microbiota. It will delve into the emerging evidence suggesting a causal connection between the gut microbiota and changes in skeletal muscle mass. Lastly, the discussion will emphasize the potential role of dietary fibre intake, known to significantly influence the composition and metabolic activity of the gut microbiota, in preventing sarcopenia.

SA13

Ubiquitin proteasome system dysfunction in insulin resistance and type 2 diabetes

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Insulin resistance is a hallmark of type 2 diabetes, which is a highly heterogeneous disease with diverse pathology. Understanding the molecular signatures of insulin resistance and its association with individual phenotypic traits is crucial for advancing precision medicine in type 2 diabetes. Underlying the development of type 2 diabetes are changes to the protein composition of tissues, termed the proteome. Proteostasis is the process that maintains a healthy proteome, cell, and ultimately the organism. Proteostasis involves a complex coordination of protein synthesis and breakdown, to ensure that damaged proteins are removed from the cell and replaced with new, functional proteins. Using proteomics, we have identified that perturbed ubiquitin-mediated proteolysis (protein breakdown) is a major driver of insulin resistance and type 2 diabetes.

SA17

Impact of between-day variability in meal pattern on energy balance and metabolic response.

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Between-day variability in meal pattern may be a novel but underexplored determinant of health. Studies exploring associations between diet and health often focus on the chemical composition of the diet, for example, the percentage of total energy from carbohydrate consumed over 24 hours. Since the 50's, and with a resurgence of interest more recently, the impact of the temporal pattern of intake has been considered potentially important with respect to health. Attempts have been made to characterise the temporal profile of intake both with respect to type and amount of food consumed. Generic terms such as 'eating incident' pattern or more commonly, 'meal pattern' have been used. Such measures as 'meal frequency', 'time of eating', eating interval' or 'time when 50% of a dietary component has been consumed' have been used to characterise the properties of an individual's temporal 'meal pattern' profile. Typically, these measures have been expressed as the mean or median of several days, (eg. mean daily meal frequency). However, using a daily mean or median obscures any between- day variability ('irregular' or 'chaotic' eating) and may mask the potential impact of between-day variability in meal pattern on health.

Recently, the potential for an individual to have an 'irregular' meal pattern has increased. This is due, in part, to greater availability of ready prepared meals, facilitating independence from established family mealtimes; greater availability of 'fast-food' outside the home; and greater variation in work shift patterns. Concurrently, obesity and associated detrimental health consequences have increased. Recent observational and intervention studies, exploring associations between 'chaotic' consumption patterns and health, have identified that this may be an underexplored, novel risk factor for obesity and its consequences, namely components of the metabolic syndrome and risk of cardiovascular disease. Energy intake regulation, or energy expenditure, for example the thermogenic response to food, may be affected, potentially independently of the nutritional composition of the diet. However, observational results are inconsistent, potentially because of differences in the measures used to describe consumption patterns, and methods used to obtain an indicator of between-day variability in pattern. A limited number of intervention studies have been undertaken, and exhibit more consistency in outcome.

The purpose of this presentation is to summarise the existing literature describing observational and intervention studies considering between-day meal pattern variability, and associations with health. The challenges posed by differences in measures of between day variability will be described. Possible mechanisms of action will be considered, with reference to chrononutrition and the potential for a 'chaotic' meal pattern to disrupt circadian entrainment.

Ali MA et al. (2024). J Hum Nutr Diet. 37, 316–353. Alhussain MH et al. (2022). Am J Clin Nutr. 115, 284-297. Alhussain MH et al, (2016). Am J Clin Nutr. 104, 21-32 Farshchi HR et al. (2005). Am J Clin Nutr. 81, 16-24. Farshchi, H et al (2004). Int J Obes 28, 653–660.

SA18

From Food processing to Oral Processing: Impact on Energy Intake, Matrix and Metabolism

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Food choice and energy intake are influenced more in the short-term by the sensory and cognitive aspects of eating than the nutritive properties of the food being consumed, yet chronic disease and ill-health result from prolonged exposure to diets low in nutrients and high in energy-density. A foods sensory and structural properties are important in shaping ‘what’ and ‘how much’ we eat, and how our metabolism responds to the nutrients and matrix-structures consumed (1). Not all calories are created equal, and research has shown how a foods texture can increase calorie intake rate (kcal/min) and increase our meal size (2). Our research has highlighted the impact of consuming food textures that can be consumed at a faster eating rate in promoting higher energy intakes in controlled feeding trials, cohort studies and nationally representative cross-sectional population based studies (3). Food texture can be applied to moderate the energy intake rate of the foods we choose to consume, and the flow of calories through our diets. In studies comparing energy intakes from minimally and ultra-processed foods, we have shown that texture based differences in meal eating rate, not degree of processing, are responsible for observed differences in energy intake at the level of the meal and the day (4-5). The relationship between processing, food-matrix properties and our metabolic responses remains poorly understood, and we have recently begun some new investigations to understand how different processes influence *in vitro* digestion and human *in vivo* metabolic responses (6). By understanding the mechanisms by which raw materials and food processing interact, we aim to influence both the rate and extent of consumption, and our metabolic response to ingested nutrients to guide the development of healthier and more sustainable foods and food processes.

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<https://doi.org/10.1007/s13668-022-00413-4>. (2) Bolhuis, D. and Forde, C.G. (2020). Application of Food Texture to Moderate Oral Processing Behaviors and Energy Intake. *Trends in Food Science and Technology*. Vol 106, 445-456 <https://doi.org/10.1016/j.tifs.2020.10.021>. (3) Teo, P.S., Whitton, C., Van Dam, R.M., Tan, L.W., L. and Forde C.G. (2021). Consuming Foods with a Higher Energy Intake Rate is Associated with Greater Energy Intake, Adiposity and Cardiovascular Risk Factors. *Journal of Nutrition*. 151(2), pp.370-378. <https://doi.org/10.1093/jn/nxaa344> (4) Teo, P.S., Tan, V.T.W., Choy, M.J., R. Janani, Lim., A., Goh, A.T., McCrickerd, K. and Forde, C.G. (2022). Texture-based differences in eating rate moderate energy intake for unprocessed and ultra-processed meals. *American Journal of Clinical Nutrition* Volume 116, Issue 1, July 2022, Pages 244–254. <https://doi.org/10.1093/ajcn/nqac068> (5) Lasschuijt M., Camps G., Mars M., Siebelink E., De Graaf K., Bolhuis D. (2023) Speed limits: the effects of industrial food processing and food texture on daily energy intake and eating behaviour in healthy adults. *European Journal of Nutrition*. 2023 Oct;62(7):2949-62. (6) Forde, C.G. and Decker, E. (2022). The Importance of Food Processing and Eating Behavior in Promoting Healthy and Sustainable Diets. *Annual Reviews in Nutrition*. 2022. 42:377–99. <https://doi.org/10.1146/annurev-nutr-062220030123>

SA19

Chrono nutrition: Integrating the 'what' with the 'when'

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At the biological level, eating schedules are predominantly dictated by endogenous timing mechanisms in multiple cells, tissues and organs. At the behavioural level, when feeding occurs at regular, anticipated times, the circadian clock initiates nutrient-sensing pathways to act synergistically to maintain nutrient homeostasis. Molecular clocks allow for temporal coordination between environmental, metabolic and behavioural cues that are caused by, or are a response to the daily perturbations in substrate availability. When feeding occurs at random times, however, these same nutrient-responsive pathways provide feedback to the circadian clocks to 'phase shift' so that on subsequent days food is anticipated at the new feeding time. Such circadian 'misalignment' acutely impacts glycaemic control through impairments to beta cell function and insulin sensitivity, predisposing to an increased risk of developing obesity and type 2 diabetes.

Periodic fasting and restricting the daily duration over which food is consumed can delay and often reverse the symptoms associated with several metabolic disorders. While the permutations in the pattern of daily food consumption are numerous, they broadly encompass three approaches: 1) sustained periods of chronic energy restriction; 2) intermittent fasting, and 3) time-restricted eating. A feature common to these dietary interventions is that perturbing feeding–fasting cycles drive robust oscillations in metabolism and circadian rhythms that confer health benefits. Indeed, a basic paradigm of circadian regulation of metabolism is that such oscillations of gene expression generate daily rhythms in cellular and whole-body metabolism.

While almost the entire body of dietary literature to date, along with the profession of nutrition science, has focused on what we eat, recent and emerging knowledge from studies that have manipulated the feeding-fasting cycle are shifting that narrative so that now it is vital that we also consider that the timing of meals plays an important role in determining metabolic health outcomes. Without consideration of both *what* and *when* is eaten, we cannot unravel the potential synergies between these two variables and their potential impact on reducing the burden of chronic metabolic diseases at the population level.

C01

Five Days of Early Time-Restricted Eating Improves Insulin Sensitivity, Appetite Regulation and Reduces Energy Intake in Young, Healthy Males

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Introduction: Altering the temporal distribution of energy intake and incorporating extended fasting periods induces metabolic effects that may improve health (Templeman *et al.*, 2020). Early time-restricted eating (eTRE), involving restricting daily energy intake to an early eating window, may be an optimal due to better alignment of eating with circadian rhythm (Clayton *et al.*, 2020). Adherence to restrictive dieting is low (Rogers *et al.*, 2016), so determining the effects of short-term adherence on health is important. This study investigated the metabolic and behavioural responses to 5-days of eTRE, in lean males.

Methods: Sixteen healthy males (age: 24 ± 3 years, BMI: 23 ± 1 kg/m², Body fat: 15 ± 3 %) completed control (CON) and eTRE trials, in random, crossover order. eTRE required adherence to an 8-hour eating window (0800-1600), and CON a 12-hour eating window (0800-2000), for 5 consecutive days. Standardised diets (2840 ± 185 kcal; 51% carbohydrate; 18% protein; 30% fat) were consumed on day-1 and day-4, and responses to a high carbohydrate breakfast (711 ± 51 kcal; 73% carbohydrate; 12% protein; 15% fat) was assessed during laboratory visits on day-2 and day-5. Blood samples were collected 0-, 1-, 2-, and 4-h post-breakfast, to assess metabolic (glucose, insulin, homeostatic model of insulin resistance (HOMA-IR) and lipids) and appetite-regulatory (acylated ghrelin (AG), glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and leptin) markers. Subjective appetite and substrate oxidation (via indirect calorimetry) were measured 0-, 1-, 2-, 3-, and 4-h post-breakfast, and ad-libitum energy intake was assessed at lunch/snack/dinner meals, taking place at 12:00/13:00-19:00/19:30 during CON, or 12:00/13:00-15:00/15:30 during eTRE. Area-under-the-curve (AUC) was calculated for blood and subjective appetite. Linear mixed models assessed differences between trials and laboratory visits, followed by Bonferroni-adjusted post-hoc pairwise comparisons, where appropriate. Study was approved by the Nottingham Trent University Human Invasive Ethics Committee (REF: 704).

Results: There were no effects for glucose ($P=0.111$), but insulin AUC was 844 ± 570 pmol/L lower and HOMA-IR was 0.18 ± 0.14 lower on day-5 during eTRE vs. CON (both $P<0.001$). Low-density lipoprotein was higher on eTRE vs. CON ($P<0.05$), with no other blood lipid differences between trials ($P>0.05$). Across both laboratory visits, total fat oxidation was 35 ± 25 % higher and total carbohydrate oxidation was 11 ± 6 % lower, during eTRE vs. CON (both $P<0.001$). GLP-1 AUC was 494 ± 759 pmol/L higher in eTRE than CON on day-5 ($P<0.05$), with no differences in PYY or AG ($P>0.05$). Leptin was greater overall during CON vs. eTRE ($P<0.05$). Energy intake was 179 ± 259 kcal lower on day-2 ($P=0.05$) and 363 ± 390 kcal lower on day-5 ($P<0.001$), during eTRE vs. CON. Hunger was lower overall during eTRE vs. CON ($P<0.001$) and reduced by 15 ± 9 % between day-2 and day-5 during eTRE ($P<0.001$).

Conclusions: Short-term adherence to eTRE can improve insulin sensitivity, increase fat oxidation, and reduce daily energy intake, and may support appetite control over time. These metabolic and behavioural effects of eTRE may be conducive to improved health and weight management long-term.

Clayton DJ, Mode WJA & Slater T (2020). *Nutr Bull* 45(4), 444–55. doi: 10.1111/nbu.12467. Lemstra M et al. (2016). *Patient Prefer Adherence* 10, 1547–1559. doi: 10.2147/PPA.S103649. Templeman I et al. (2020) *Proc Nutr Soc* 79(1), 76-87. doi: 10.1017/S0029665119000636.

C02

Sex differences in the postprandial lipid response to sucrose

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High fructose intakes can increase postprandial lipaemia and are associated with an increased incidence of metabolic disorders such as type 2 diabetes and cardiovascular disease (Chong, Fielding, & Frayn, 2007; Geidl-Flueck & Gerber, 2023). It has been demonstrated that females display a higher hepatic *de novo* lipogenesis in response to a high-fructose meal compared with males, yet this did not translate into increased postprandial lipaemia (Low *et al.*, 2018). Furthermore, other data suggest females display a lower postprandial lipaemia in response to a mixed meal (Pramfalk *et al.*, 2015), and therefore potential sex differences in the lipaemic response to different sugars are currently unclear. Accordingly, the aim of the present study was to assess sex differences in the postprandial lipaemic response to ingestion of a drink containing either sucrose (high-fructose) or maltodextrin (glucose-only polymer).

In a randomised, double-blind, cross-over design, expired breath and plasma samples were collected from 24 healthy participants (12 female and 12 male) for 360 minutes after ingestion of a drink containing 50 g fat (spiked with 200 mg [U-13C]palmitate) with 100 g of either maltodextrin (MD) or sucrose (SU). Normality of data were checked by visual inspection of residuals. Total and incremental area under the curve were calculated for each outcome and used to analyse differences between sexes within each condition using both an independent t-test and ANCOVA with fat free mass (FFM) as a covariate.

Males had a higher TAG iAUC (mean±95%CI) concentration compared to females after SU ingestion (128.0±73.2 mmol/L*360min vs 47.79±27.61 mmol/L*360min, $p=0.02$) but there was no sex difference after MD ingestion (72.39±55.41 mmol/L*360min vs 28.95±16.17 mmol/L*360min, $p=0.13$). After MD and SU ingestion females had higher plasma glucose iAUC concentrations (MD 306.5±78.0 mmol/L*360min vs 117.0±123.5 mmol/L*360min, $p=0.005$; SU 200.5±84.6 vs 108.0±47.4, $p=0.02$ SU) and higher plasma insulin iAUC concentrations (MD 59.87±17.0 umol/L*360min vs 33.5±11.8 umol/L*360min, $p=0.005$; SU 34.97±10.1 umol/L* 360min vs 16.01±5.2 umol/L*360min, $p<0.001$) compared to males but this did not remain when FFM was added as a covariate (glucose MD 236.63±98.7 mmol/L*360min vs 241.03±92.18 mmol/L*360min, $p=0.9$; glucose SU 199.01±101.89 mmol/L*360min vs 109.34±95.16 mmol/L*360min $p=0.3$; insulin MD 48.86±21.04 umol/L*360min vs 44.51±21.04 umol/L* 360min, $p=0.8$; insulin SU 34.95±12.04 pmol/L*360min vs 16.03±12.04 pmol/L*360min, $p=0.8$). After SU ingestion females had higher plasma lactate iAUC concentrations compared to males (308.9±50.1 mmol/L*360min vs 218.8±52.8 mmol/L*360min, $p=0.007$) but this did not remain when FFM was added as a covariate (289.71±78.55 mmol/L*360min vs 236.35±73.36 mmol/L*360min, $p=0.42$). There were no meaningful sex differences in plasma VLDL-rich TAG [S_r 20-400] tAUC, plasma NEFA tAUC, plasma BHB tAUC concentrations, total fat and carbohydrate oxidation, or total exogenous fat oxidation with or without FFM as a covariate ($p>0.05$ for all).

These data demonstrate that despite a larger relative dose of fat and sugar, females display a lower lipaemic response than males following high-sugar oral fat tolerance tests. These responses cannot be explained by differences in whole-body or exogenous fat oxidation rates, and therefore further research on the mechanisms of sex differences in response to sugar intake is warranted.

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C03

A high fat isocaloric diet enriched with saturated fat compared to polyunsaturated fat increases cardiometabolic disease risk factors in metabolically healthy humans

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Background: Emerging evidence suggests the type of dietary fat consumed, irrespective of the amount, may increase intrahepatic triglyceride (IHTG) content, which is a risk factor for cardiometabolic disease (CMD). Previous work demonstrated hypercaloric diets enriched with saturated fat (SFA), compared to unsaturated fat, led to greater IHTG accumulation, despite similar weight gain (1, 2). However, it remains unclear how dietary fat composition influences IHTG accumulation and CMD risk in the absence of weight change.

Aim: To investigate the effects of isocaloric diets enriched with either SFA- or n-6 polyunsaturated fats (PUFA) on IHTG content and CMD risk factors in metabolically healthy men and women.

Methods: 14 adults underwent a baseline MRI scan to measure IHTG content and postprandial metabolic study day, afterwards they were randomly assigned to consume an isocaloric high-fat (HF) diet enriched in either SFA or n-6 PUFA for up to 24 days, before undergoing a post-diet MRI scan and postprandial metabolic study day. Food diaries were collected and analysed using Nutritics software. Fasting and postprandial plasma biochemistry and substrate oxidation rates were measured during metabolic study days.

Results: 6 individuals (2 females, age:48.2±5.5 years, BMI:26.6±2.9 kg/m²; mean ± SD) consumed a high-SFA diet while 8 individuals (3 females, age:50.3±8.6 years, BMI 26.2±3.8 kg/m²) consumed a high-PUFA diet. At baseline, participants randomised to the SFA-enriched HF diet consumed 88±19 g of fat/day, (35.0±2.4% total energy (TE)), of which 33±11 g/day (12.9±2.6%TE) was SFA; during the experimental dietary intervention, lasting 18 (13-24) days (median(range)), participants consumed 135±34 g of fat/day, (47.4±6.2%TE), of which 66±17 g/day (23.3±4.8%TE) was SFA. At baseline, participants randomised to the PUFA-enriched HF diet consumed 95±24 g of fat/day, (38.7±7.8%TE), of which 10±3 g/day (4.1±0.8%TE) was PUFA; during the experimental dietary intervention, lasting 20 (13-23) days, participants consumed 133±54 g of fat/day, (50.9±7.1%TE), of which 27±7 g/day (10.9±3.4%TE) was PUFA. There was no change in body weight from baseline (SFA: 81.2±16.9 kg vs. 81.2±16.6 kg; PUFA: 82.7±16.4 kg vs. 82.9±16.4 kg) with consumption of either isocaloric SFA- or n-6 PUFA-enriched HF diet.

Fasting and postprandial plasma biochemistry were measured before and after consumption of the isocaloric HF diets. Consuming a SFA-enriched HF diet increased fasting total cholesterol (p=0.0046), high-density lipoprotein (HDL) (p=0.013), non-HDL cholesterol (p=0.032), and decreased non-esterified fatty acids (p=0.003) compared to baseline, while consuming a PUFA-enriched HF diet decreased fasting total cholesterol (p=0.026), non-HDL cholesterol (p=0.0096)

and plasma triglyceride (TG) ($p=0.055$) compared to baseline. Neither HF diet significantly altered IHTG, fasting glucose, or insulin, nor changed postprandial TG, NEFA, or very low-density lipoprotein-TG from baseline. There was no change in net fat and carbohydrate oxidation from fasted to fed state, before and after either HF diet, or between experimental groups.

Conclusion: These preliminary results show, despite no change in body weight, dietary fat composition modulates fasting cholesterol, non-HDL cholesterol, and TG, suggesting the type of dietary fat consumed, irrespective of the total amount, may play an important role in influencing well-established CMD risk factors and future CMD risk.

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C04

The effects of 24-hour fasting and carbohydrate restriction on postprandial glucose and lipid metabolism in healthy adults

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Intermittent fasting is a popular dietary strategy involving repeated bouts of substantial energy restriction (ER). Over ~24 hours, fasting induces marked alterations in metabolic substrate utilisation that are partially a consequence of low carbohydrate (CHO) availability. Few studies have explored the effects of acute fasts on postprandial glucose and triglyceride (TAG) responses (Antoni et al., 2016; Clayton et al., 2018), which are independent predictors of cardiometabolic risk. This study investigated the effects of a 24-hour fast and a time-matched period of low CHO intake without ER on postprandial glucose and TAG concentrations in healthy volunteers.

In a randomised crossover design, 16 healthy adults (13 males, body mass index 24.8±3.3 kg/m², mean±SD) completed three 24-hour dietary conditions in counterbalanced order: i) fasting (FAST; 0 kcal); ii) CHO restriction without ER (LCHO, ≤20g CHO; 1923±339 kcal); iii) control diet without ER (CONT, >150g CHO; 2004±360 kcal). Participants consumed a mixed-macronutrient liquid meal standardised to 1/3 of their resting metabolic requirements immediately after each condition. Fasting capillary beta-hydroxybutyrate (BHB) concentrations were measured, and blood samples were collected at baseline and regular postprandial intervals for 120min to quantify plasma glucose and TAG concentrations. Time-course data were analysed using two-way repeated measures ANOVA. Area under the curve (AUC) and BHB data were analysed using one-way repeated measures ANOVA. Significant effects were followed up with paired t-tests and application of Ryan-Holm-Bonferroni stepwise corrections.

Plasma glucose concentrations displayed a significant time x condition interaction effect ($p=0.026$). Glucose incremental AUC (iAUC) increased after FAST (148.7±146.0 mmol/L*120min) compared to LCHO (81.4±81.5 mmol/L*120min, $p=0.029$) and CONT (55.8±46.3 mmol/L*120min, $p=0.027$). Plasma TAG responses diverged between conditions (time x condition, $p=0.012$) and were highest after CONT and lowest after FAST. Decreases in TAG concentrations were observed at 60min (0.691±0.229 mmol/L, $p=0.028$) and 120min after (0.856±0.320 mmol/L, $p=0.023$) FAST, and at 120min after LCHO (0.950±0.525 mmol/L, $p=0.021$) relative to CONT (60min 0.975±0.472 mmol/L; 120min 1.195±0.519 mmol/L). TAG total AUC was lower after FAST (88.1±27.9 mmol/L*120min, $p=0.018$) and LCHO (99.6±12.1 mmol/L*120min, $p=0.017$) compared to CONT (115.1±49.2 mmol/L*120min), while TAG iAUC decreased after FAST (5.5±9.0 mmol/L*120min, $p=0.028$) relative to CONT (20.5±19.1 mmol/L*120min, $p=0.028$) and LCHO (16.5±15.0 mmol/L*120min, $p=0.036$). Fasting BHB increased after FAST (0.4±0.2 mmol/L, $p=0.002$) and LCHO (0.2±0.2 mmol/L, $p=0.006$) compared to CONT (0.1±0.1 mmol/L).

These findings demonstrate that a 24-hour period of low CHO intake, with or without ER, reduces postprandial TAG concentrations in healthy adults, an effect previously observed after 36-hour complete or partial ER in participants with overweight and obesity (Antoni et al., 2016). Low CHO

availability alters hepatic fatty acid partitioning towards increased β -oxidation and ketogenesis, thus away from TAG export into the circulation within very low-density lipoproteins, providing an explanation for the reduction in postprandial TAG concentrations. Repeated periods of fasting and CHO restriction may be clinically relevant in postprandial lipid management independently from weight loss, with longer-term studies needed to explore their application in populations at increased cardiometabolic risk. Whether regular fasting negatively impacts glycaemic control also warrants further investigation, particularly in populations with existing impairments in glucose tolerance.

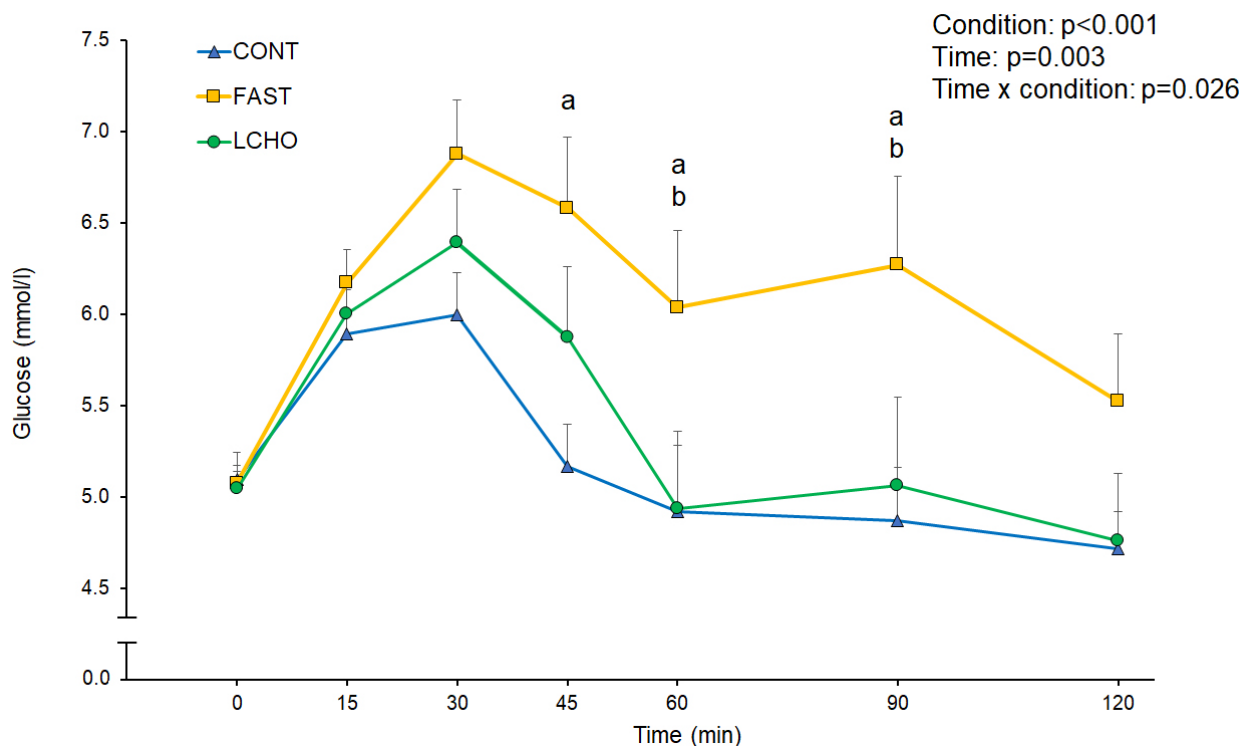


Figure 1: Postprandial (2-hour) glucose responses to a liquid mixed-macronutrient meal after 24-hour control (CONT), fasted (FAST) and low carbohydrate (LCHO) conditions. Significant differences ($p < 0.05$) between CONT vs FAST are annotated with a, and between LCHO vs FAST with b. Data are means ($n=16$) and SEMs. Comparisons were made using two-way repeated measures ANOVA, with significant effects followed up with paired t -tests (Ryan-Holm-Bonferroni stepwise corrections applied).

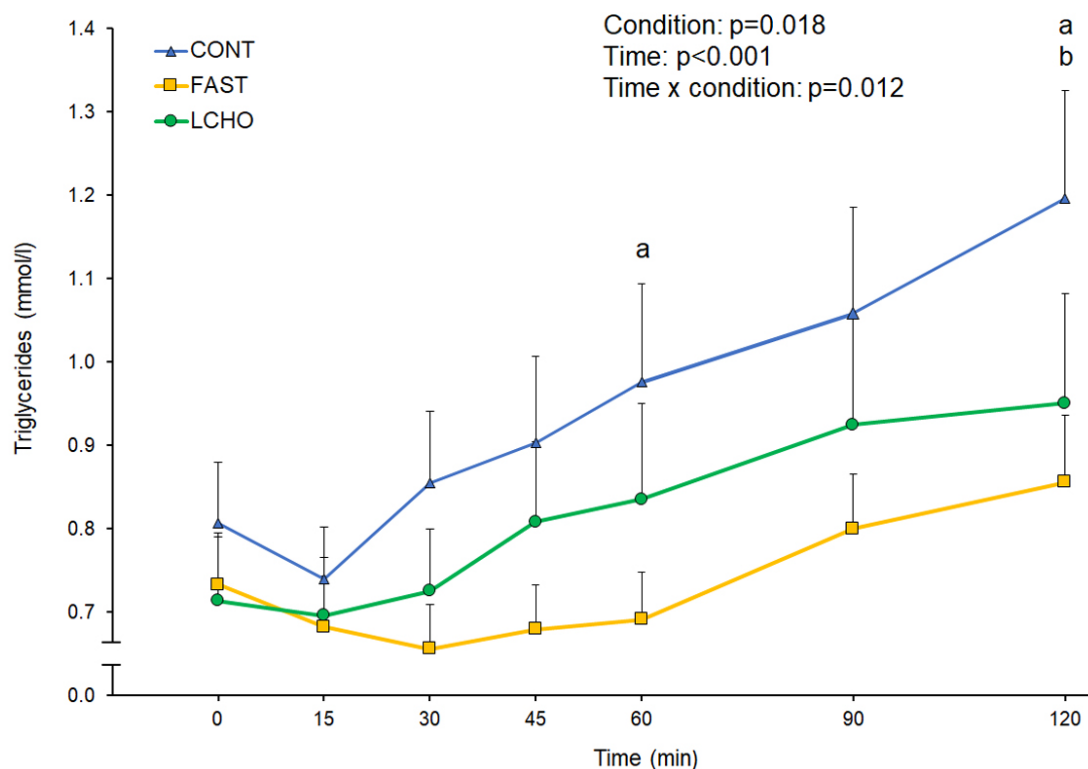


Figure 2: Postprandial (2-hour) triglyceride responses to a liquid mixed-macronutrient meal after 24-hour control (CONT), fasted (FAST) and low carbohydrate (LCHO) conditions. Significant differences ($p<0.05$) between CONT vs FAST are annotated with a, and between LCHO vs FAST with b. Data are means ($n=16$) and SEMs. Comparisons were made using two-way repeated measures ANOVA, with significant effects followed up with paired t -tests (Ryan-Holm-Bonferroni stepwise corrections applied).

Antoni R et al. (2016). Br J Nutr 115, 6, 951-9. Clayton DJ et al. (2018). Br J Nutr 120, 10, 1107-1116.

C05

Exogenous ketosis increases post-prandial hepatic de novo lipogenesis in adults free from metabolic disease

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Ingestion of the ketone monoester (KME), thereby inducing a state of exogenous ketosis, reduces post-prandial glucose concentrations in healthy individuals¹. Glucose is a principle substrate for hepatic *de novo lipogenesis* (DNL) with elevated availability increasing DNL². Here we explored the hypothesis that exogenous ketosis-induced blood glucose suppression would reduce post-prandial DNL.

Ten adults free from metabolic disease (6F/4M; age: 28 ± 2 yr; BMI: 23.8 ± 1.1 kg·m⁻²; mean \pm SEM) underwent two 7 hr postprandial study days. After an overnight fast, participants consumed a mixed-nutrient breakfast meal that provided 2 g·kg⁻¹ bodyweight of carbohydrate (891.7 ± 80.9 kcal; 65.5% total kcal from carbohydrate, 10.0% protein, 24.5% fat). At 1 hr post-meal, either a KME (573 mg·kg⁻¹) or a taste and volume-matched placebo (PLA) drink was consumed in a blinded and randomised-counterbalanced crossover manner. For two days prior to each visit, participants undertook a eucaloric high-sugar prescribed diet (404 ± 31 g·day⁻¹ carbohydrate; 55.5% as sugar) to drive increased DNL. Heavy water (D₂O) was consumed the evening preceding and during each study visit to achieve ~0.4% plasma enrichment. Venous blood samples were collected at fasting and for 7 hr post-prandially. Hepatic DNL was quantified as the incorporation of deuterium into newly synthesised palmitate (16:0) within very low-density lipoprotein-triglyceride (VLDL-TG), determined by gas-chromatography mass-spectrometry. Data were analysed by paired t-tests and two-way (time & condition) repeated-measures ANOVAs. All results are presented as mean \pm SEM with significance at $p < 0.05$.

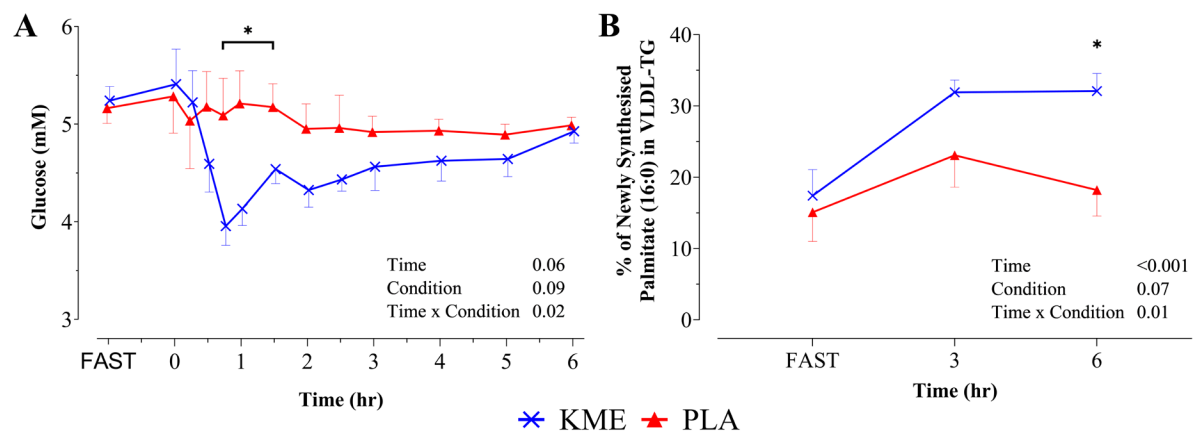
Plasma [β -hydroxybutyrate] was elevated by KME with greater concentrations observed from 15 to 300 min post-drink ($p \leq 0.03$; KME: 3.14 ± 0.42 , PLA: 0.05 ± 0.01 mM). Plasma glucose concentrations were reduced after the KME drink (**Fig. 1A**), with area-under-the-curves 7.4% lower compared to PLA ($p < 0.001$). Post-prandial insulinaemia was unaffected by KME. There were distinct differences in hepatic DNL, such that KME increased DNL at 360 min post-drink (absolute increase, 13.9%; $p = 0.01$) with a tendency to also be greater at 180 min (8.8%, $p = 0.09$; **Fig. 1B**). KME did not affect plasma [VLDL-TG] nor the proportion of palmitate (16:0) or other fatty acids (14:0, 16:1n-7, 18:0, 18:1n-9, 18:2n-6) within VLDL-TG (mol%). Both plasma [non-esterified fatty acid] and [glycerol] were suppressed during the latter stages of the feeding test under KME ($p \leq 0.04$). There were no differences between KME and PLA conditions for plasma [triglyceride], [cholesterol], [high-density lipoprotein], or [lactate], nor for respiratory quotient.

The current study demonstrates that post-prandial hepatic DNL is elevated under exogenous ketosis in healthy adults, despite lowered circulating glucose levels and insulin being unaffected. This might have pathological implications as Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)³ and hepatic insulin resistance⁴ are associated with elevated DNL. Future work

investigating the influence of chronic exposure to exogenous ketosis on DNL, as well as in patient populations with MASLD and type 2 diabetes, is warranted.

Figure Caption:

FIGURE 1. A, Circulating glucose (mM). **B,** DNL as the proportion of newly synthesised palmitate (16:0) in VLDL-TG (%). * $p < 0.05$ between KME and PLA.



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C06

β -alanine Supplementation in Adults with Overweight or Obesity: A Randomised Placebo-Controlled Feasibility Trial

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Introduction: Overweight and obesity are characterised by accumulation of excess adiposity and a subsequent systemic, chronic, low-grade inflammation, which is associated with a range of metabolic disorders including dyslipidaemia and hyperglycaemia (Calder et al., 2011). Our recent meta-analysis suggested that supplementation with carnosine, or its rate-limiting precursor β -alanine, reduces fasting glucose and HbA1c in humans and rodents with overweight, obesity, or diabetes (Matthews et al., 2021). The primary aim of the study was to assess the feasibility and acceptability of chronic β -alanine supplementation in adults with overweight or obesity; with a secondary aim to explore the effect of supplementation on markers of glycaemic control.

Methods: Thirty participants with overweight or obesity (BMI: ≥ 25 to < 40 kg/m²; $n=9$ with prediabetes: HbA1c 42-47 mmol/mol) were randomised (stratified for age, sex, BMI, and HbA1c) to receive 4.8 g/day of sustained-release β -alanine ($n=14$, age 57 ± 11 y, BMI 30.6 ± 2.9 kg/m², HbA1c 39.5 ± 4.0 mmol/mol) or a matched-placebo ($n=13$, age 59 ± 10 y, BMI 31.6 ± 3.0 kg/m², HbA1c 40.2 ± 4.6 mmol/mol) for 3-months. Twenty-seven participants completed the trial. Adherence (1-month, 2-months, follow-up) and side effects (baseline, acute response to supplementation, 1-month, 2-months, and follow-up) were recorded. Fasting blood samples were taken using venepuncture from the ante-cubital fossa at baseline and follow-up, and biomarkers of glycaemic control were analysed: HbA1c, glucose, insulin, C-peptide, homeostatic model assessment (HOMA) of β -cell function (HOMA2-%B) and insulin resistance (HOMA-IR). Ethical approval was granted by Nottingham Trent University and NHS Health Research Authority (REC reference: 21/NW/0280) research ethics committees, in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. Data were analysed using a Bayesian approach involving informative and non-informative prior distributions, and estimation of posterior probabilities.

Descriptive statistics are presented as mean \pm 1SD; inferential data presented as median [95% credible intervals (CrI)]. Trial preregistration: NCT05329610.

Results: *Feasibility outcomes:* high-dose β -alanine was well-tolerated over 3-months; evidenced by high adherence rates (β -alanine: 0.92 [0.85 to 0.95], placebo: 0.91 [0.84 to 0.95]), low attrition (6.7% and 13.3%), and participant-reported side effects which remained below baseline values and comparable across groups. *Exploratory outcomes:* results did not show clear evidence in favour of or against supplementation for glycaemic control outcomes: HbA1c (-0.06 [-0.30 to 0.15 mmol/mol]), fasting glucose (-0.02 [-0.50 to 0.45 mmol/L]), C-peptide (-30.1 [-211.7 to 151.3 pmol/L]), insulin (-7.4 [-15.3 to 0.32 pmol/L]), HOMA2-%B (-5.5 [-14.3 to 3.5]), or HOMA-IR (-0.18 [-0.48 to 0.11]) (Figure 1).

Conclusion: The present study shows that 3-months of β -alanine supplementation is well-tolerated and does not cause adverse events in adults with overweight and obesity. We did not find clear evidence that supplementation affected markers of glycaemic control; however, our feasibility estimates suggest that a fully powered study to detect meaningful effects would need to be large. Researchers should consider alternative approaches or more advanced conditions, such as prediabetes or type-2 diabetes.

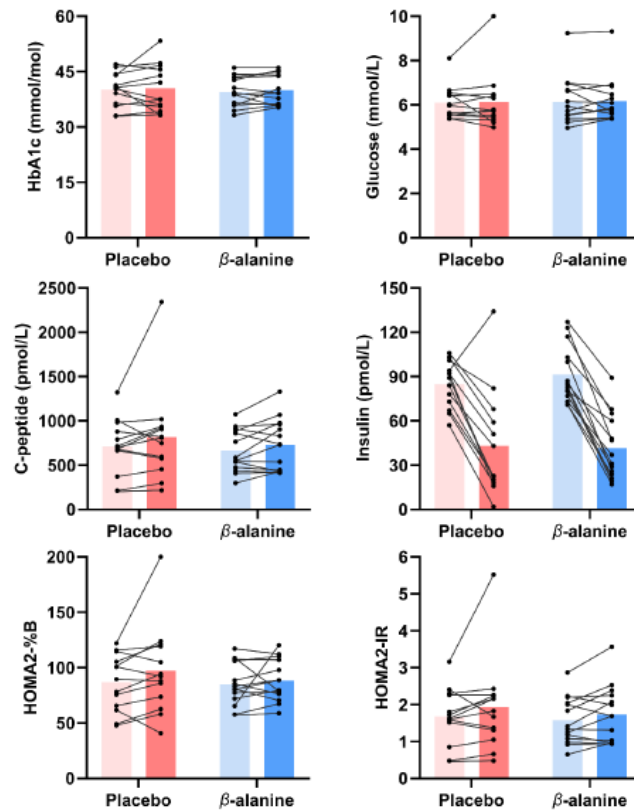


Figure 1. Pre- and post- β -alanine supplementation values for markers of glycaemic control. Data presented as mean values with individual data points. Statistical model inferential data are presented in the main text.

Calder PC et al. (2011). *Br J Nutr* 106(S3), S1-78. Matthews JJ et al. (2021). *Adv Nutr* 51(10), 2098-108.

C07

No effect of dietary nitrate supplementation on mitochondrial respiration in young healthy adults

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Dietary nitrate (NO_3^-) supplementation increases systemic nitric oxide (NO) bioavailability, and can reduce the oxygen cost of submaximal exercise and enhance exercise tolerance. However, the influence of dietary NO_3^- supplementation on the efficiency of mitochondrial respiration is unclear. **Purpose:** To investigate the effects of acute and chronic dietary NO_3^- ingestion on mitochondrial respiration in young healthy adults. **Methods:** Using a randomized, double-blind crossover design, 8 participants (6 males: 27 ± 7 years, 2 females: 23 ± 1 years) consumed NO_3^- rich beetroot juice (BR) (~ 12.8 mmol NO_3^-) and NO_3^- depleted placebo beetroot juice (PL) (~ 0.08 mmol NO_3^-) acutely and then chronically every day for 2 weeks, separated by at least 1-week washout period. Skeletal muscle samples were collected from vastus lateralis at 3 h following supplement ingestion on day 1 and day 14. 2-3 mg permeabilized muscle fibres, 2 ml mitochondrial respiration medium, and 25 ml oxygen were added to a two-channel, high-resolution Oroboros Oxygraph-2K (Oroboros, Oxygraphy, Innsbruck, Austria) prior to analysis. Glutamate and malate, Adenosine 5'-diphosphate (ADP), cytochrome c, succinate, carbonyl cyanide 4 phenylhydrazone (FCCP), rotenone and antimycin A were injected to measure leak respiration, maximal oxidative phosphorylation (OXPHOS) and uncoupled electron transfer capacity. The OXPHOS-leak control efficiency (P-L control efficiency) was calculated as the 1-leak respiration/OXPHOS (1-L/P). Two-way repeated ANOVA was used to assess the differences in mitochondrial respiration between groups (PL vs BR) and across time (acute vs chronic). **Results:** There were no significant differences in leak respiration (acute PL: 7.17 ± 1.21 pmol O_2 mg^{-1} sec^{-1} , acute BR: 6.99 ± 1.48 pmol O_2 mg^{-1} sec^{-1} , $P=0.75$; chronic PL: 8.72 ± 3.70 pmol O_2 mg^{-1} sec^{-1} , chronic BR: 8.02 ± 2.28 pmol O_2 mg^{-1} sec^{-1} , $P=0.65$) and P-L control efficiency (acute PL: 0.83 ± 0.05 , acute BR: 0.84 ± 0.05 , $P=0.76$; chronic PL: 0.83 ± 0.05 , chronic BR: 0.86 ± 0.04 , $P=0.26$) between BR and PL ingestion. Similarly, no differences in maximal OXPHOS (acute PL: 46.89 ± 16.63 pmol O_2 mg^{-1} sec^{-1} , acute BR: 46.19 ± 11.51 pmol O_2 mg^{-1} sec^{-1} , $P=0.86$; chronic PL: 54.02 ± 20.40 pmol O_2 mg^{-1} sec^{-1} , chronic BR: 59.63 ± 22.40 pmol O_2 mg^{-1} sec^{-1} , $P=0.52$) and uncoupled electron transfer capacity (acute PL: 56.04 ± 15.85 pmol O_2 mg^{-1} sec^{-1} , acute BR: 59.34 ± 10.85 pmol O_2 mg^{-1} sec^{-1} , $P=0.44$; chronic PL: 64.51 ± 19.63 pmol O_2 mg^{-1} sec^{-1} , chronic BR: 70.08 ± 24.23 pmol O_2 mg^{-1} sec^{-1} , $P=0.61$) were found between BR and PL supplementation. **Conclusion:** Neither acute nor chronic dietary NO_3^- ingestion improved mitochondrial respiration in young healthy adults. These results indicate that the lower oxygen cost of submaximal exercise that has been reported previously following dietary NO_3^- ingestion is not related to enhanced mitochondrial respiration efficiency.

C08

iPREVENT: Increasing colonic propionate as a method of preventing weight gain in adults aged 20-40 years, a 12-month randomised controlled trial.

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One in four UK adults is obese. In 2021 the total cost of overweight and obesity in the UK was estimated at £98 billion¹. Presently, emphasis is placed on strategies for obesity treatment rather than proactive prevention. Although strong evidence suggests that preventing weight gain in early adulthood when weight gain is fastest, is critical for reducing obesity risk and preventing chronic disease later in life. High daily fibre intake is inversely associated with body weight. Fibre may exert this effect via enhanced fermentation by bacteria in the colon and the production of short-chain fatty acids (SCFAs), which have been shown to confer a health *benefit* on the *host*. However, only 10% of the UK population reaches the recommended intake of 30g of fibre per day and therefore forfeits the beneficial effects of SCFA production. We developed a novel food ingredient, inulin-propionate ester (IPE), to target delivery of the SCFA propionate to the colon, releasing propionate equivalent to the fermentation of 60g of fibre in 10g IPE. Our previous clinical studies in overweight, middle-aged adults demonstrated that IPE prevented weight gain and lowered abdominal adiposity over six months.

This randomised, parallel-group, placebo-controlled, double-blind trial aimed to investigate the effect of increasing colonic propionate concentrations using IPE on preventing weight gain in young adults aged 20 to 40 years old. The secondary objectives were designed to investigate whether the increase in colonic propionate via IPE could beneficially affect body composition and cardiometabolic biomarkers.

We recruited 270 (n=135 per arm) young adults who were overweight and demonstrated behaviours associated with weight gain. Participants were randomised to either 10 g IPE or 10 g inulin control, consumed daily for 12 months.

At 12 months, body weight was 78.9 kg ± 11.8 (n=114) and 81.4 kg ± 11.9 (n=112) for inulin and IPE, respectively, resulting in a non-significant baseline-adjusted mean difference in weight gain of 1.02 (95% CI: -0.37 to 2.41) kg for IPE versus inulin control. Amongst secondary outcomes, the adjusted difference in means for fat-free mass; 1.07 kg (0.21 to 1.93), body water; 0.72 kg (0.1 to 1.33) and fasting glucose; 0.11 mmol/L (0.01 to 0.21), were statistically significant, being higher for IPE compared with the inulin control.

In conclusion, contrary to prior evidence, IPE did not prevent weight gain in this cohort of younger adults at greatest risk of weight gain. These results suggest that younger adults may respond to IPE differently compared with middle-aged participants from previous studies. However, it is noteworthy that the IPE-consuming participants had augmented fat-free mass, suggesting that propionate may have a distinct effect on body composition. Future research should explore

differences in the colonic environment, metabolism, and appetite between younger and older adults.

1 Frontier Economics. Unhealthy Numbers: The Rising Cost of Obesity in the UK. 2023.
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C09

In young South Asian and White European women, an acute dose of cocoa flavanols may augment forearm vasodilation evoked by mental stress, but not exercise, or reactive hyperaemia

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Cocoa flavanols (CFs) are proposed to decrease the risk of cardiovascular disease (CVD) by reducing blood pressure, and augmenting endothelium-dependent dilatation (EDD), by increasing nitric oxide (NO) bioavailability (1). Evidence suggests EDD is blunted in young South Asian (SA) compared to White European (WE) men (2), consistent with higher CVD risk in SAs (3). Whether EDD is blunted in SA women has received little attention, nor has the effect of CFs on EDD in young women.

Thus, healthy women (11 WE/12 SA, aged 18-26years) completed food frequency and lifestyle questionnaires before undertaking a double-blind, cross-over study, in which they randomly received high-(695mg CFs) and low-flavanol (5.6mg CFs) cocoa drinks across two visits during the low-oestrogen phase of their menstrual cycle. One hour later, near-infrared spectroscopy (NIRS) was applied to the forearm to monitor totalHb (oxyHb+deoxyHb), as an index of forearm blood flow following 2-min arterial occlusion (reactive hyperaemia), 2-min rhythmic handgrip at 60% maximal voluntary contraction (exercise hyperaemia) and during 8-min mental stress (arithmetic) task. Effects of ethnicity and CFs on Δ totalHb were compared by two-way repeated measures ANOVA.

Physical inactivity was more prevalent amongst SAs than WEs (41.7% vs 0% with <1day physical activity/week, $p=0.0373$). Further, WEs consumed more fibre (WE:19.7 \pm 5.67(mean \pm SD), SA:14.4 \pm 5.05g/day, $p=0.0269$), vitamin C (WE:133 \pm 42.3, SA:89.5 \pm 44.1mg/day, $p=0.0241$), and fruit than SAs (WE:7.91 \pm 0.680, SA:4.50 \pm 0.657times/week, $p=0.0017$). Peak reactive hyperaemia tended to be higher in WEs (WE:65.5 \pm 45.3, SA:42.6 \pm 15.9AU, $p=0.0595$), as was peak exercise hyperaemia (WE:57.1 \pm 36.1, SA:31.3 \pm 16.1AU, $p=0.0113$). However, acute CFs had no effect on reactive (high-CF:50.3 \pm 38.0, low-CF:55.7 \pm 30.7AU, $p=0.507$), or exercise hyperaemia (high-CF:47.8 \pm 36.6, low-CF:39.3 \pm 22.0AU, $p=0.275$).

During mental stress, Δ totalHb was not different between WE and SA women and acute CFs had no effect on this response in either group ($p>0.305$), in contrast to the augmented forearm vasodilatation reported in men (4). However, whereas some individual women showed the expected forearm vasodilator response to mental stress, others showed vasoconstriction as reported previously, particularly in SA men (2). Since the proportion of “vasodilators” and “vasoconstrictors” was comparable in WE and SA women (both 50%), effects of CFs were tested in these subgroups. There was no effect of CFs in “vasodilators”, but the mean decrease in totalHb was attenuated in “vasoconstrictors” ($p=0.005$), consistent with CFs promoting vasodilation.

These findings indicate that both reactive and exercise hyperaemia are blunted in young SA, relative to WE women. We propose this may partly reflect lower physical activity and cardioprotective nutrient intake in SA women, lifestyle behaviours known to impair EDD. Assuming

CFs increase NO availability (1), the lack of effect of acute CFs on reactive, and exercise hyperaemia suggests any contribution NO makes to these responses is small, or already maximal in both young SA and WE women, possibly reflecting influences of oestrogen. The forearm vasodilator response to mental stress is largely NO mediated (5), while exaggerated vasoconstrictor responses to stress are predictive of CVD (2). Against this background, we suggest that irrespective of ethnicity, CFs may be particularly beneficial in increasing NO availability in women whose forearm vasodilator response to mental stress is impaired.

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C10

Investigating the impact of fatty acids and insulin on hepatocellular autophagic flux and inflammatory activation in metabolic dysfunction-associated steatotic liver disease (MASLD)

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterised by the pathological accumulation of intrahepatocellular triglyceride (IHCTG). Although initially benign, IHCTG may lead to inflammatory activation and progression to steatohepatitis and more severe liver disease. Hyperinsulinemia and dietary fat quantity and composition have been associated with MASLD development and progression which may be mediated through an aberrant decrease in autophagy. The aim of this work was to determine the effects of insulin concentration and fatty acid (FA) quantity and composition on hepatocellular autophagic flux and inflammatory activation in an *in vitro* model of IHCTG accumulation.

Methodology: Huh7 hepatocyte cells were cultured for 7 days in low fat-low sugar (LFLS) or high fat-high sugar (HFHS) media with either predominantly unsaturated or saturated FA compositions and at 0.1 or 100 nmol insulin concentrations. IHCTG was extracted from cells and analysed using gas chromatography. Autophagic flux was quantified by Western Blotting through accumulation of LC3-II with and without autophagic inhibition and media cytokines were measured using Olink® Target 48 Cytokine Panel. Results from six biological repeats and analysed with two-way ANOVA followed by pairwise t-tests with BH correction for multiple comparisons.

Results: Cells cultured in HFHS compared to LFLS media had higher IHCTG concentration ($p < 0.0001$) and the IHCTG composition reflected the FAs cells were cultured in. Compared to cells cultured in LFLS media, cells cultured in HFHS media (saturated or unsaturated FAs) had higher secretion of chemokines (CXCL9, CCL3, and CCL4) but cells cultured in HFHS media with unsaturated FAs also had a higher secretion of CXCL10, IL6 and CXCL8 ($p < 0.01$) and tended ($p = 0.074$) to have a lower autophagic flux. There were no other differences in autophagic flux between conditions and insulin had no effect on either IHCTG accumulation, composition or cytokine secretion.

Conclusions: Higher FA quantity increased inflammatory activation, especially with unsaturated FAs which may have been mediated by a decrease in autophagy. Hyperinsulinemia had limited effects on this model which may suggest that hepatocytes adapt better to changes in insulin concentration than to changes in FA quantity or quality.

C11

Endothelium dependent dilatation and effects of transition to university life on diet of first year biomedical students

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Cardiovascular disease (CVD) prevalence is greater in those of South Asian (SA) ethnicity than White Europeans (WE), SA women being at particular risk of early ischaemic heart disease (1,2). Correspondingly, we showed in university students, that endothelium-dependent dilatation (EDD), a prognostic indicator of CVD (3) is blunted in young SA, relative to WE women; SA women also had lower physical activity levels and fruit/vegetable intake (4), which are risk factors for CVD. University students generally have unhealthy eating habits: only ~18% of UK students meet the UK recommended daily allowance (RDA) of 5 fruit/vegetable portions/day (5). We have now tested the effect of transition to university on 1st year students recruited to an intervention study, in which we will test the effects of improving the diet.

Female students (24 SA; 21 WE), aged 18.75±1.03, 19.00±1.14 years respectively (mean±SD), who volunteered for the intervention study, completed the EPIC food frequency, International Physical Activity questionnaires (FFQ, IPAQ respectively) and Perceived Stress Scale questionnaire at the beginning of semester 1. In addition, near infrared spectroscopy was applied to forearm to monitor total haemoglobin (THb), an index of blood flow, and oxygen saturation (SO₂) in muscle during and following 2-min arterial occlusion (reactive hyperaemia), which reflects EDD. Participants repeated all 3 questionnaires at the end of Semester 1.

There were no differences between WE and SA women for BMI (22.25±3.25 vs 21.96±4.80; mean±SD) or mean arterial blood pressure (77.05±18.50 vs 71.19±12.80mmHg) (P=0.81, 0.22 respectively, un-paired t-test). In contrast to our recent findings (1), there were also no differences between WE and SA women for peak reactive hyperaemia or tissue SO₂ (Figure 1). Further, there were no differences between WEs and SAs for IPAQ (2745±1968 vs 3220±2369 MET min/week; P=0.47), fruit/vegetable (2.40±1.35 vs 2.35±1.5 portions/day; P=0.92) or vitamin C (111.6±57.94 vs 101.1±54.93 mg/day; P=0.54).

Finally, when WEs and SAs were grouped together, there were no differences between the beginning and end of Semester 1 for IPAQ (2998±2180 vs 2377±1607 MET min/week; P=0.12; paired t-test) or Perceived Stress scores (18.18±6.24 vs 19.40±6.44; P= 0.12), both being in the moderate range. Fruit/vegetable intake did not change (2.37±1.42 vs 2.55±1.63 portions/day; p=0.58). However, total energy (1823±679.3 vs 1466±567.3 kcal/day; P=0.006), carbohydrate (221.0±85.62 vs 175.0±71.70g/day; P=0.007), Vitamin C (106.0±55.96 vs 79.15±55.72mg/day; (P=0.02) and fibre (16.93±9.30 vs 12.98±7.61g/day; P=0.04) decreased by the end of semester 1, to below the RDA, protein decreasing from (81.83±36.01 vs 64.99±26.56g/day; P=0.006).

We suggest that the present finding that physical activity, dietary intake and indices of EDD did *not* differ between young WE and SA women on entry to university, may be explained if WE women with poorer lifestyle choices self-selected for a dietary “improving” intervention study. If so, then the

blunted EDD reported in young SA relative to WE women (2) may partly reflect lifestyle choices of SA women rather than genetics. Irrespective, the present findings indicate that the diet of WE and SA female students who already have a poor diet on entry to university deteriorates during transition to university and requires attention.

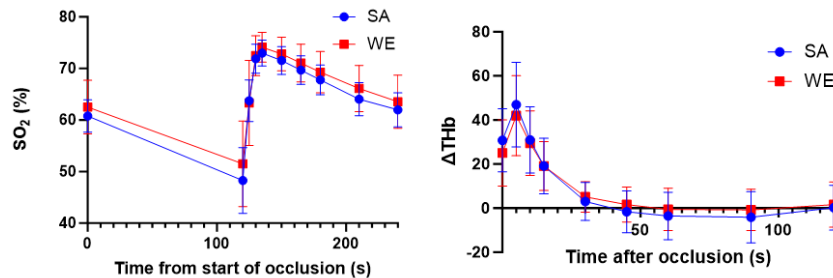


Figure 1: Reactive hyperaemia in young SA and WE women. Values are NIRS-derived tissue SO_2 during arterial occlusion and reactive hyperaemia (left) and change from baseline in THb (ΔTHb), an index of blood flow, during reactive hyperaemia (right). WE and SAs compared by un-paired t-tests.

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C12

Systematic review of evidence that environmental contaminant exposure impedes weight loss and glycaemic control during calorie-restricted diets in humans and animals

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Introduction

Chemical exposure has been linked to obesity and type 2 diabetes (T2DM) development and thus may also limit success of weight loss diets for obesity and T2DM management.

Aims

We aimed to determine the effect of environmental chemical exposure on mass loss and glycaemic control during diet-induced weight management.

Method

We systematically searched PubMed, Web of Knowledge, and Scopus. Study selection, screening and data extraction followed preferred reporting items for systematic review and meta analysis (PRISMA) guidelines. The protocol is registered in PROSPERO (CRD42022339993). Independent selection and screening were performed by 2 evaluators. Risk of bias was performed using established tools and nested meta-analysis of comparable studies performed using the `rma.mv` function in the `metafor` package in R.

Results

We retrieved 178 unique records from databases, and 34 from citing and cited papers. Six papers directly examined impacts of environmental contaminant exposure on diet-induced weight loss and/or glycaemic control in humans and five in animals. One targeted people with T2DM. In humans, one paper linked phthalates and parabens, but not bisphenols, with slower fat loss. Two showed per- and polyfluoroalkyl substances (PFAS) were not associated with mass loss, but with faster subsequent mass regain. One explored BMI improvements in relation to air pollutants. Two papers reported weight loss-induced elevation in plasma organochlorines associated with altered glycaemic control. There were insufficient papers on any one contaminant group to perform meta-analyses for human studies. Risk of bias was moderate to serious, primarily from potential for deviation from intended diet, and statistics and reporting.

In rodents, high fat diet was used to induce obesity and impaired glycaemic control. One paper examined PFAS, one examined the organochlorine pesticide, dichloro-diphenyl-trichloroethane (DDT), and three explored polychlorinated biphenyl 77 (CB77). Perfluoro-octane sulphonate (PFOS) impaired glycaemic control, but not weight loss, in obese male C57BL/6 mice. DDT did not impair weight loss in Sprague Dawley rats. CB77 did not affect final mass of C57BL/6 mice after four

weeks of calorie restriction (standardised mean difference = -0.35 [-0.87, 0.18]; n = 5 (experiments); n = 3 (papers)), but impaired glucose control in glucose tolerance tests (standardised mean difference = -1.30 [-1.80, -0.79]; n = 6 (experiments); n = 3 (papers)) and insulin tolerance tests (standardised mean difference = -1.54 [-2.32, -0.77] n = 3 (experiments); n = 2 (papers)). Heterogeneity was low and did not differ between animal models ($I^2 = 0$; $\tau^2 = 0$; $p > 0.1$) but experiments on CB77 were underpowered and came from the same research group. All studies were at moderate to serious risk of bias, largely due to lack of reported detail.

Conclusions

Human and animal studies suggest some chemical groups, especially PCB and PFAS, could impair management of body mass and glucose control, but the evidence is sparse and at high risk of bias. Studies that robustly address whether chemical exposure can impair weight loss and resumption of glycaemic control are urgently needed to help determine whether chemical exposure history should be considered when delivering care for obesity and T2DM.

C13

Supplementing short-term aerobic exercise with nitrate-rich beetroot juice accelerates improvements in cardiorespiratory fitness and blood pressure in postmenopausal women with overweight or obesity: A pilot study.

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Background: Post-menopausal women are at high risk of impaired cardiometabolic health due to age and inactivity-related declines in cardiorespiratory fitness, excess abdominal adiposity, and reduced oestrogen concentrations which contribute to vascular aging and endothelial dysfunction [1]. Despite low uptake, regular engagement in aerobic exercise is most effective at mitigating low cardiorespiratory fitness, cardiometabolic associated co-morbidity, and premature mortality. Previous studies also suggest inorganic nitrate (NO_3^-) supplementation can enhance cardiorespiratory fitness, both in post-menopausal women [2] and those with obesity [3], and may attenuate effort and pain perception during exercise [4], indicating its potential as an adjunctive therapy to support exercise involvement and potentiate improvements in cardiometabolic health. However, this remains relatively unexplored. **Aim:** To assess whether supplementing a short-term (3-wk) aerobic exercise training programme with NO_3^- -rich beetroot juice accelerates improvements in cardiorespiratory fitness and parameters of cardiometabolic health and inflammation. **Methods:** 12 inactive, self-identified post-menopausal women ($\text{BMI} > 25 \text{ kg/m}^2$) completed 9 moderate-intensity (65% $\text{VO}_{2\text{peak}}$) exercise sessions on a cycle ergometer, which progressively increased in duration (30–60 minutes), either with (Ex+BRJ; $n=7$) or without (Ex; $n=5$) daily consumption of a NO_3^- -rich beetroot juice shot (8.2 mmol/d; Beet it Sport Shot, James White Drinks Ltd, United) in a single-blinded, parallel manner. At baseline and immediately following the protocol, anthropometrics, body composition (BIA), and resting systolic and diastolic BP (sphygmomanometer) were assessed and a submaximal exercise test completed to extrapolate maximal oxygen consumption ($\text{VO}_{2\text{peak}}$), the gold standard indicator of cardiorespiratory fitness [5]. Fasted blood samples were collected to assess cardiometabolic (glucose, insulin, HOMA-IR, TAG, HDL-C, LDL-C, TC:HDL) and inflammatory markers (IL-6, TNF- α). Paired and independent samples t-tests (two-tailed) were used to detect significant changes (α level $p < 0.05$) within (pre-post intervention) and between groups, respectively. Where data was not normally distributed, Wilcoxon Signed Rank and Mann-Whitney U tests were employed. Data presented as mean \pm SD. **Results:** $\text{VO}_{2\text{peak}}$ increased $7.0\% \pm 3.8\%$ ($+1.7 \pm 0.9 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $p=0.002$) in Ex+BRJ but remained unchanged in Ex ($+0.6 \pm 2.1 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $p=0.534$), however, no between-group differences were observed ($p=0.248$). Resting systolic BP reduced in Ex+BRJ ($-9.8 \pm 2.8 \text{ mmHg}$, $p < 0.001$) and Ex ($-6.6 \pm 2.5 \text{ mmHg}$, $p=0.004$), with the decline tending to be greater in Ex+BRJ (-3.2 mmHg , $p=0.064$). A minor reduction in body fat ($-0.8 \pm 0.8\%$, $p=0.040$) and fasting plasma IL-6 ($-0.45 \pm 0.14 \text{ pg} \cdot \text{mL}^{-1}$, $p=0.049$) was seen in Ex+BRJ, but not in Ex (both $p > 0.05$). No other changes in body composition, RPE, blood lipids, glucose metabolism, or inflammatory markers were observed. **Conclusions:** Preliminary data suggests supplementation with NO_3^- -rich beetroot juice may potentiate improvements in cardiorespiratory fitness and certain indices of cardiometabolic health seen with short-term aerobic exercise alone. Further, larger-scale studies, with greater statistical power are needed to consolidate our findings and determine the potential of NO_3^- -rich beetroot juice as an exercise therapeutic in post-menopausal women with overweight or obesity.

The study protocol complied with the Declaration of Helsinki, with ethical approval granted by The MVLS Ethics Committee at The University of Glasgow.

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C14

Three months of beta-alanine supplementation on haemodynamic and biochemical markers of myocardial function and health in adults with overweight or obesity

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Introduction

Overweight and obesity are major global public health concerns, associated with an increased risk of developing cardiovascular disease (CVD). Carnosine is a pleiotropic histidine-containing dipeptide synthesised from beta-alanine and L-histidine. Intramuscular carnosine content can be increased via supplementation with carnosine or its rate-limiting precursor beta-alanine (Harris et al., 2006). Emerging evidence in animal models suggests that carnosine may play a role in cardiovascular health by exerting beneficial effects on calcium handling and excitation-contraction coupling (Gonçalves et al., 2021), as well as haemodynamic parameters (Niiijima et al., 2002; Aldini et al., 2011). Therefore, this study aimed to explore three months of beta-alanine supplementation on cardiovascular function and health in adults with overweight or obesity, exploring the potential influence on haemodynamic and biochemical markers.

Methods

Initially, 30 adults with overweight or obesity (BMI: ≥ 25 to < 40 kg/m²) were enrolled on the trial, with 27 successfully completing the intervention. Participants were blinded and randomised (stratified for age, sex, BMI, and HbA1c) to receive 4.8 g·day⁻¹ of sustained-release beta-alanine ($n = 7$ male, 7 female; age, 57 ± 11 y; BMI, 30.6 ± 2.9 kg/m²) or a taste and appearance-matched tapioca starch placebo ($n = 8$ male, 5 female; age, 59 ± 10 y; BMI, 31.6 ± 3.0 kg/m²) for 3 months. Non-invasive continuous haemodynamic measurements were performed on participants pre- and post-supplementation, using a CNAP Monitor which assessed continuous finger blood pressure, advanced haemodynamics, and dynamic fluid response parameters. Venepuncture was completed pre- and post-supplementation to measure lipid and CVD-related biomarkers, including total cholesterol, low-density lipoproteins, high-density lipoproteins, triglycerides and high sensitivity C-reactive protein. All procedures were conducted in accordance with the ethical

standards of the NHS Health Research Authority and Nottingham Trent University research committees and the principles of the Declaration of Helsinki. Data were analysed using a Bayesian approach involving non-informative prior distributions, and estimation of posterior probabilities. Descriptive statistics are presented as mean \pm 1SD; inferential data are presented as median [95% credible intervals (CrI)]. Trial preregistration: NCT05329610.

Results

Participants were supplemented for 87 ± 8 days in the beta-alanine group and 87 ± 4 days in the placebo group. For both biochemical and haemodynamic outcomes, results did not show clear evidence in favour or against supplementation. The descriptive and inferential statistics of these outcomes are presented in **Table 1**.

Conclusion

There was no clear evidence in favour or against three months of beta-alanine supplementation at $4.8 \text{ g} \cdot \text{day}^{-1}$ on haemodynamic and biochemical markers of myocardial function and health in adults with overweight or obesity. A study with longer beta-alanine supplementation and/or in patients with established CVD comorbidities may be necessary to further explore any therapeutic potential of beta-alanine supplementation on cardiovascular and cardiometabolic parameters.

Table 1. Haemodynamic and cardiac-related biochemical markers pre- and post-supplementation.

	Placebo		Beta-alanine		Intervention Effect Placebo:Beta-alanine	Probability > 0
	Pre	Post	Pre	Post		
Haemodynamic Parameters						
Systolic BP (mmHg)	138 \pm 13	133 \pm 20	132 \pm 15	132 \pm 16	2.2 (-11.4 to 15.9)	0.629
Diastolic BP (mmHg)	80 \pm 8	77 \pm 13	75 \pm 8	77 \pm 10	2.7 (-6.8 to 12.2)	0.721
Mean arterial BP (mmHg)	102 \pm 8	99 \pm 14	99 \pm 11	100 \pm 11	2.8 (-7.1 to 12.8)	0.717
Resting Heart Rate (bpm)	64 \pm 10	63 \pm 11	67 \pm 13	63 \pm 10	-2.7 (-7.4 to 2.1)	0.128
Cardiac Output (L/min)	6.0 \pm 0.9	6.2 \pm 1.4	6.1 \pm 1.3	5.7 \pm 0.9	-0.53 (-1.2 to 0.2)	0.061
Cardiac Index (L/min/m ²)	2.9 \pm 0.4	3.0 \pm 0.4	3.0 \pm 0.6	2.8 \pm 0.4	-0.18 (-0.47 to 0.10)	0.093
Stroke Volume (mL/min)	95.7 \pm 20.5	100.0 \pm 25.6	92.2 \pm 17.8	92.1 \pm 16.2	-4.7 (-13.2 to 3.9)	0.138
Stroke Volume Index (mL/min/m ²)	46.4 \pm 7.8	48.2 \pm 8.5	45.5 \pm 7.4	45.8 \pm 7.0	-1.7 (-5.5 to 2.1)	0.187
SVR (dyne*s/cm ⁵)	1293 \pm 277	1240 \pm 328	1244 \pm 303	1328 \pm 279	122.6 (-60.7 to 296.4)	0.908
SVR Index (dyne*s*m ² /cm ⁵)	2617 \pm 431	2497 \pm 522	2483 \pm 469	2652 \pm 442	217.7 (-122.3 to 569.4)	0.898
Pressure Pulse Variation (%)	6.1 \pm 3.4	5.3 \pm 2.0	6.5 \pm 2.2	6.9 \pm 3.2	1.5 (-0.57 to 3.5)	0.924
Stroke Volume Variation (%)	12.7 \pm 7.6	10.5 \pm 3.9	11.8 \pm 3.1	10.9 \pm 3.9	0.78 (-2.0 to 3.4)	0.715
Biochemical Parameters						
Total cholesterol (mmol/L)	5.0 \pm 1.5	5.0 \pm 1.6	5.3 \pm 1.0	5.1 \pm 1.2	-0.20 (-0.77 to 0.39)	0.242
LDL (mmol/L)	3.0 \pm 1.1	3.0 \pm 1.2	3.1 \pm 0.9	3.0 \pm 1.1	-0.09 (-0.54 to 0.38)	0.341
HDL (mmol/L)	1.3 \pm 0.4	1.3 \pm 0.4	1.3 \pm 0.3	1.3 \pm 0.3	-0.01 (-0.09 to 0.07)	0.408
Triglycerides (mmol/L)	1.4 \pm 0.5	1.4 \pm 0.5	1.3 \pm 0.4	1.3 \pm 0.6	-0.05 (-0.31 to 0.23)	0.361
TC:HDL ratio	4.1 \pm 1.0	4.1 \pm 1.1	4.1 \pm 0.9	4.0 \pm 1.2	-0.04 (-0.44 to 0.36)	0.416
HDL:LDL ratio	2.5 \pm 0.8	2.4 \pm 0.9	2.4 \pm 0.8	2.4 \pm 1.0	0.03 (-0.30 to 0.36)	0.565
hs-CRP (mg/L)	2.3 \pm 1.9	1.9 \pm 1.1	4.5 \pm 6.0	3.4 \pm 3.5	1.2 (-0.85 to 3.3)	0.886

Data presented as mean \pm 1 standard deviation; intervention effect data presented as median [95% credible interval]. Abbreviations: BP, blood pressure; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; SVR, systematic vascular resistance.

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C15

Inadequate folate and selenium intake in retired concussed rugby union players: link to accelerated cognitive decline

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Introduction:

Cognitive abilities decline with age [1]. In addition, repeated concussions in retired rugby union players may increase the risk of cognitive decline [2]. Evidence suggests that adequate dietary intake of selenium and folate protects against cognitive decline and dementia [3]. Low intake of both nutrients is associated with increased oxidative stress which may contribute to cognitive decline [4]. However, dietary assessment in retired union rugby players has not been investigated.

Methods:

Twenty retired rugby union players aged 64 ± 5 years having sustained 3 concussions incurred over 22 years were compared to 21 sex, age-, cardiorespiratory fitness- and education-matched controls with no prior participation in contact sports or concussion history. A self-administered validated semi-quantitative food frequency questionnaire (FFQ) was used to estimate typical food intake over the past 12 months. The Montreal Cognitive Assessment (MoCA) was employed to assess cognition. Dietary data were converted into estimated nutrient intakes using a nutritional software package (Q-Builder, Tinuviel Software; Anglesey, UK). Following confirmation of distribution normality (Shapiro Wilks W tests), between-group differences were assessed using independent samples t -tests. Data are expressed as mean \pm standard deviation (SD) and significance established at $P < 0.05$.

Results:

Compared to controls, players consumed fewer calories, carbohydrates, protein, folate and selenium (Table 1). Players were characterised by lower MoCA scores than controls (24 ± 3 points vs. 26 ± 2 points, $P = 0.020$), consistent with mild cognitive impairment (MCI).

Conclusion:

Collectively, these findings demonstrate that retired rugby union players are characterized by inadequate selenium and folate intake. Lower dietary selenium intake has been associated with declined cognitive function and increased risk of dementia [1, 3]. Folate plays a key role in reducing serum homocysteine concentration, the latter a modifiable risk factor for cognitive decline and dementia [5]. Selenium and folate supplementation may confer neuro-prophylactic benefits in

retired players with concussion history and attenuate their trajectory towards accelerated brain ageing.

Table 1: Dietary intake

	Controls (n=21)	Players (n=20)	P Value	Guidelines UK ¹
Calories (kcal)	2,316 ± 529	1,948 ± 547	0.035	2,330
Carbohydrate (g)	284 ± 94	225 ± 69	0.012	-
Fat (g)	90 ± 21	76 ± 29	0.078	-
Protein (g)	97 ± 22	83 ± 23	0.043	-
Folate (µg)	415 ± 103	327 ± 81	0.040	200 µg
Selenium (µg)	58 ± 17	45 ± 14	0.012	75 µg

Values are mean ± SD; $P < 0.05$ vs. controls. ¹Department of Health, 1991.

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C16

Preliminary findings from a project to explore the efficacy and mechanisms for blackcurrants to reduce risk of type 2 diabetes

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Preliminary findings from a project to explore the efficacy and mechanisms for blackcurrants to reduce risk of type 2 diabetes

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Elevated postprandial glucose is a primary risk factors for developing insulin resistance in individuals with overweight or obesity. Both acute ingestion and short-term supplementation of anthocyanins improves postprandial glucose responses to a high-carbohydrate meal. However, the optimal anthocyanin dose is not yet known. In vitro studies suggest that the glucose-lowering effects of anthocyanins may act by enhancing the expression of proteins associated with glucose uptake and mimicking the action of insulin. The precise mechanism by which anthocyanins exert their beneficial effect on glucose metabolism in skeletal muscle remains to be determined.

Purpose. This project has two aims: 1) to examine the dose-response effects of short-term supplementation with anthocyanin-rich New Zealand blackcurrant (NZBC) extract on postprandial glucose responses to a high carbohydrate challenge, 2) and to investigate the potential mechanism by which anthocyanins to improve skeletal muscle glucose uptake.

Methods. In a randomised, double-blind, counterbalanced Latin-square design, five overweight (BMI > 25 kg m²) sedentary individuals completed four separate oral glucose tolerance tests after ingesting no dose (PLA), or one of three doses (300, 600, or 900 mg day⁻¹) of NZBC extract (CurraNZ™) for 7 days. Parallel experimentation using murine C2C12 myotubes enabled insights into the biochemical mechanisms by which anthocyanins may improve glucose uptake. Cells were either untreated (CON) or treated with NZBC, insulin (INS) or NZBC + INS and lysed for the isolation of RNA and subsequent determination of mRNA transcripts by RT-qPCR.

Results. The data demonstrate a pattern whereby PLA > 300 > 600 > 900 mg for the area-under-the-curve for plasma glucose (PLA: 678 257, 300mg: 623 203, 600mg: 583 169, 900mg: 527 128 mmol L⁻¹120 min⁻¹) and were 8.1%, 14.0% and 22.3% lower than the placebo condition, respectively. At this stage the data is too underpowered to perform any statistical analysis. In vitro, the presence of the NZBC extract enhanced the mRNA expression of GLUT4 (10-fold), Hexokinase 2 (6-fold), and Myocyte Enhancer Factor (2-fold), thereby suggesting an adaptive remodelling of the apparatus within skeletal muscle responsible for glucose uptake.

Conclusion. Together, these preliminary data indicate that repeated intake of NZBC extract increases glucose tolerance. Our findings suggest a role for anthocyanins in skeletal muscle adaptative remodelling, although others have proposed that anthocyanins interact with key targets

involved in insulin signalling pathways. Further, in-vitro studies are warranted to delineate the precise mode of action by which anthocyanins improve glucose uptake.

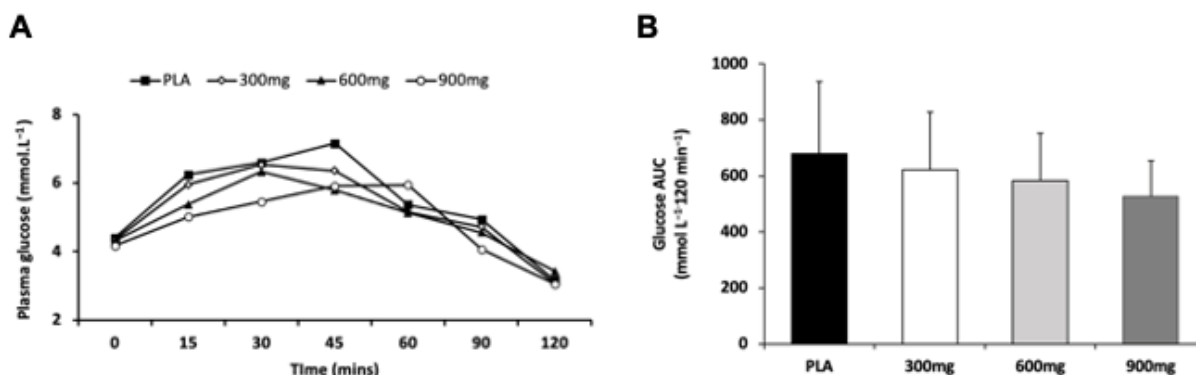


Figure 1. Effect of short-term supplementation with NZBC extract or placebo on glucose tolerance and insulin sensitivity. Concentration time-course responses of plasma glucose (A) to an oral glucose tolerance test, and the corresponding area under the curve (B), following short-term (7 days) supplementation with NZBC extract (300 mg, 600mg, 900mg anthocyanins per day) or placebo). Values are presented as means \pm S.D. (n=5). Current data is underpowered to show significance.

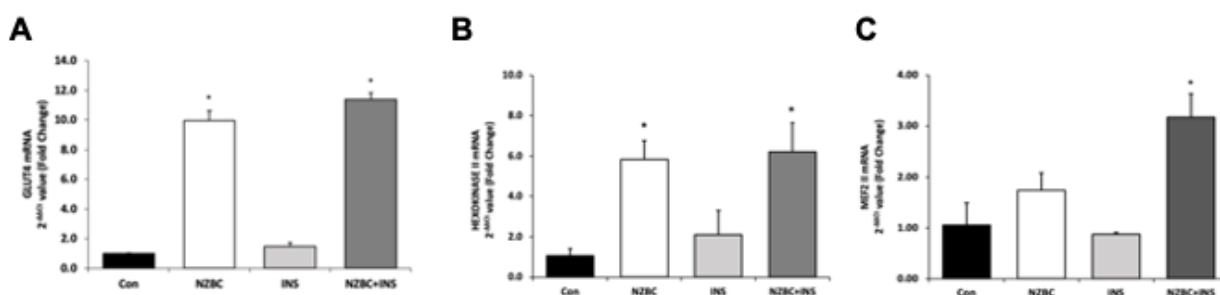


Figure 2. Skeletal muscle gene expression after treatment with NZBC extract.

Gene expression analysis ($\Delta\Delta C_t$) of C2C12 skeletal muscle cells differentiated in control media (CON), or treated with NZBC extract (10 μ g/ml), or exposed to insulin (INS; 100 nM) or a combination of both (NZBC; 10 μ g/ml + INS 100 nM) for 4 hours. A, GLUT4; (B) Hexokinase II; (C) Myocyte Enhancer Factor 2 (MEF2). Insulin was used as a positive control, however it should be noted that the time-course by which insulin exerts its effect is more rapid and therefore the data should be interpreted accordingly. *Significantly different from unstimulated sample ($P < 0.05$).

C17

Does increasing lean red meat intake improve iron status in iron-deficient physically-active females?

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Background: Female athletes and active adult females engaging in high volumes of exercise are at increased risk of compromised iron status due to heightened iron losses through menstruation, as well as exercise-induced mechanisms associated with physical training [1,2]. Oral iron supplementation is commonly employed in the prevention and/or treatment of iron deficiency but has been criticised because of associated side effects, such as constipation and increased risk of iron toxicity [1]. There is increasing interest in the use of food-based approaches, such as the prescription of an iron-rich and/or heme iron-based diet, for improving and maintaining iron status in females [3,4]. Therefore, the aim of the present study is to investigate the effects of increased lean red meat consumption on iron status in iron-deficient physically-active females in comparison to a habitual diet or an oral iron supplement (clinical trial registration: ISRCTN43345245).

Methods: Physically-active iron-deficient non-anaemic females are randomly assigned at a ratio of 1:2:2 to either a control condition (CON), oral iron supplementation (SUPP), or an increase in lean red meat consumption (MEAT) for 12 weeks. Participants in the CON group maintain their habitual diet. Participants in the SUPP group consume their habitual diet with the provision of an oral iron supplement (325 mg of dried ferrous sulphate, equivalent to 105 mg elemental iron) ingested on alternate days for the intervention period. Participants in the MEAT group supplement their habitual diet with portions of lean red meat (170 g uncooked) consumed on alternate days for the intervention period. Iron status (hemoglobin, hematocrit, serum iron, serum ferritin, serum transferrin receptor, transferrin, transferrin saturation, total iron binding capacity), body composition (sum of 8 skinfolds, bioelectrical impedance analysis), dietary intake (4 day portion-estimate food diary), and subjective ratings of fatigue are measured before (week 0), during (weeks 4 and 8) and after (week 12) the intervention period.

Results: Preliminary results (CON, n=4; SUPP, n=7; MEAT, n=5) show similar baseline values for iron status across all 3 groups, with serum ferritin concentrations of 27.3 ± 13 ng/mL, 21.3 ± 10.4 ng/mL, and 25.4 ± 10.9 ng/mL for CON, SUPP and MEAT, respectively. Serum ferritin concentrations are unchanged in CON, but are increased directionally by week 8 in SUPP and MEAT. Recruitment for this study is ongoing with an expected completion date of June 2024.

Conclusion: This study is investigating the effects of increased lean red meat consumption on iron status in iron-deficient physically-active females. Preliminary results indicate that this food-based approach has the potential to improve iron status in a similar magnitude to iron supplementation in this population.

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C18

Dose-response effect of pre-exercise protein ingestion on fat oxidation: a secondary analysis

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Fuel substrate selection during exercise is influenced by several factors including nutritional status, sex and fitness (1). Compared to pre-exercise carbohydrate consumption, exercising in a fasted state results in higher fat oxidation rates. Therefore, fasted exercise is a popular training strategy for exercisers who aim to increase fat oxidative capacity. Less is known about the influence of pre-exercise protein consumption on fuel substrate selection. We and others have previously reported that pre-exercise protein consumption might not affect fat oxidation rates compared to fasted exercise (2,3,4). This study is a secondary analysis from previously published data (4) where we aimed to establish whether the effect of different pre-exercise protein doses on fat oxidation rates during exercise were influenced sex, fitness and body composition.

In a double-blinded randomised within-subject study design, fifteen healthy active individuals (9 males, 6 females, age: 25 ± 5 yr, height: 175 ± 10 cm, weight: 73.4 ± 13.1 kg, VO_{2max} : 46.8 ± 9.0 mL/kg/min) performed one hour of cycling at 60% of their peak power, thirty minutes after having consumed either 0, 20 or 40 grams of whey protein hydrolysate. Indirect calorimetry was used to measure substrate oxidation every 15 min of exercise. Body composition, using bio-electrical impedance and fitness using a ramp-test protocol were completed during a screening visit. Two and three-way ANOVA were used for statistical analysis with time and treatment as within-subject factors and sex as between-subject factor. ANCOVA was deployed to adjust fat oxidation rates for fitness (VO_{2max}). Outcomes are Mean \pm SE.

Overall, fat oxidation increased over time during exercise (0.15 ± 0.04 , 0.23 ± 0.03 , 0.30 ± 0.03 , 0.32 ± 0.03 g/min at 15, 30, 45 and 60 min respectively; $p = 0.000$), but no treatment (0 gr = 0.23 ± 0.03 , 20 gr = 0.25 ± 0.04 , 40 gr = 0.27 ± 0.04 , g/min $p = 0.16$) or interaction effect ($p = 0.32$) was observed. Including VO_{2max} as a co-variate had no effect on the outcomes (all p -values > 0.05). There was no overall effect of sex (F: 0.21 ± 0.05 , M: 0.29 ± 0.4 g/min; $p = 0.24$) or treatment*sex ($p = 0.73$). No significant effects were observed when fat oxidation was expressed relative to body weight (g/min/kg BW; treatment-effect: $p = 0.15$) or fat-free mass (g/min/kg FFM; treatment-effect: $p = 0.17$).

Consumption of different doses of protein before exercise seems to maintain similar fat oxidation rates compared to fasted exercise and was not affected by sex, fitness and body composition. Therefore, pre-exercise protein ingestion might be considered as a feeding strategy for exercisers who aim to enhance fat oxidative capacity but struggle to incorporate fasted training into their program.

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C19

Beneficial medicinal effects of the green vegetable fruit of *Momordica charantia* (bitter melon) to treat non-communicable diseases when used uncooked.

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Introduction: People have used plants as both food and medicine since their existence. One such plant is *Momordica charantia* (*M-charantia*) or bitter melon. **Aims and objectives:** This study investigated the potential beneficial cost-effective use of daily consumption of *M-charantia* fruit juice (volume/weight) in conjunction with diet modification and daily exercise in newly diagnosed type 2 diabetic (T2DM), obese and hypertensive patients. The effect of the alcoholic extract of *M-charantia* was also investigated in cancer cell lines. The study had the relevant ethical clearance from the University of Guyana and University of Central Lancashire to undertake the study.

Method: Fresh *M-charantia* fruits were purchased from local markets, washed and cut into small pieces and blended (without the seeds) in either water (volume/weight) or in 70% alcohol. The blended fruit juice with water was consumed (20g/ml) daily by either diabetic, obese or hypertensive patients (n=10 for each intervention) over 6 weeks. The blood glucose, weight and blood pressure were measured before the consumption of the juice, and then weekly after for 6 weeks. Daily exercise and diet modification were facilitated by either a professional sport scientist or a dietitian. Blood samples were taken prior to the consumption of the juice and 6 weeks later for analysis. For cancer study, cell lines were treated with different concentrations of the alcohol extract dissolved in DMSO in comparison to cisplatin for comparison. Data were analyzed using Student's t-test and presented as mean \pm SEM. **Results:** The daily intake of *M-charantia* alone decreased fasting blood glucose level (FBGL (mg/dl)) significantly ($p<0.05$) in a time-dependent manner, like diet modification and daily exercise, *M-charantia* combined with diet modification and daily exercise and *M-charantia* combined with 60 mg daily of diamicon MR. After 6 weeks of treatment, FBGL decreased by 47.7%, 33.4%, 50.6% and 50.7%, respectively for the 4 interventions compared to the start of each intervention. The effect of *M-charantia* on FBGL was dose-dependent. Likewise, *M-charantia* consumption, combined with daily exercise, can reduce body mass index (BMI) moderately, but significantly with blood pressure in a time-dependent manner, either with or without amlodipine (5 mg daily). *M-charantia* also decreased HbA1c, systolic (SBP) and diastolic (DBP) blood pressure, total lipids, and triglycerides (TGL) significantly ($*p<0.05$) after 6 weeks compared to week 1. HbA1c was reduced from 12.18 \pm 1.4 to 5.58 \pm 0.39* (%), FBGL from 200.6 \pm 11.20 to 125.8 \pm 11.20* (mg/dl), SBP from 200.60 \pm 11.20 to 125.8 \pm 11.20 mm Hg, DBP from 89.45 \pm 7.29* to 79.40 \pm 9.20* mm Hg, total lipids from 240.50 \pm 19.10 to 191.90 \pm -9.20* (mg/dl) and TGL from 187.20 \pm 20.19 to 139.80 \pm 10.70* (mg/dl). Chemical analysis of *M-charantia* revealed that *M-charantia* is rich in cations including Na⁺, K⁺, Ca²⁺, Mg²⁺, Mn²⁺, Cu²⁺, and Zn²⁺, proteins (2.86 \pm 0.07 mg/100g), phenolic content (2.42 \pm 0.25 mg/100 g) and antioxidants, especially ceulic acid (6.23 \pm 0.60 ng/g). In cancer cell line studies, *M-charantia* alcoholic extract killed triple breast cancer cell lines compared with cisplatin, but not healthy breast cancer cell line. **Conclusions:** The results suggest that *M-charantia* can be used cost-effectively to treat diabetes, obesity, blood pressure and cancer.

