A pre-meal drink of low-dose whey protein (WP) microgel rapidly increases bioavailability of branched chain amino acids (BCAA) in people with type 2 diabetes (T2D): a randomized, placebo-controlled crossover study

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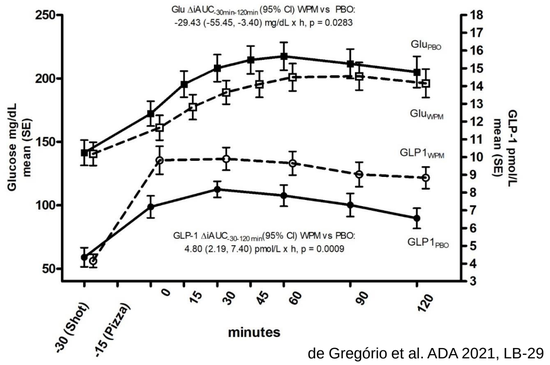
BACKGROUND

- People with type 2 diabetes (T2D) and overweight or obesity often have impaired postprandial (PP) metabolic control.
- Whey proteins (WP), found in dairy products, are rich in AAs and peptides that can stimulate insulin secretion, but their routine use has been limited by requiring a high dose (25-50g), and consumption well in advance of a meal (approx 30 min).
- New micelle-technology [WPM] allowing for a more rapid absorption, could enable a greater potency of WP.
- We recently demonstrated that, compared to placebo, 125 mL of 10 g WPM taken 15 min ahead of a pizza meal significantly altered the early PP glucose trajectory and reduced the 2h incremental area under the curve (iAUC) by 22% while at the same time increased the total GLP-1 response by 66% (Figure)

Fig. Effects on PP glucose and GLP-1 response with pre-meal intake of WPM in people with type 2 diabetes



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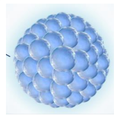
OBJECTIVE

- To assess the effects of WPM on free plasma BCAA trajectories
- Schematic illustration of the highly concentrated WPM sturcture



METHODS

- This crossover study in drug-naïve or metformin-treated T2D with overweight or obesity, studied the effects of 10g WP (40kcal) prepared as WPM, or placebo (PBO, 0kcal [water – for volume equivalence]), provided as a 125mL shot 15min ahead of a 250g pizza meal (622kcal [29.0g protein, 22.6g fat, 72.6g carbohydrates]).
- PP BCAA trajectories were evaluated in a post-hoc analysis in frequently drawn blood-samples over a 2h period.
- ClinicalTrials.gov: NCT04639726

METHODS (CONT.)

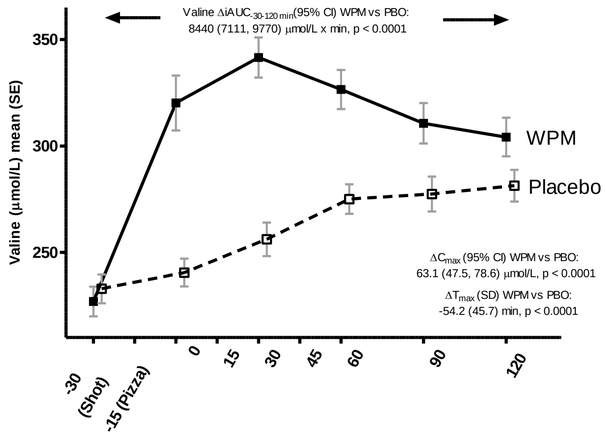
- The differences between WPM and PBO were assessed by comparing change in iAUC as well as by comparing maximum concentrations reached (Cmax) by mixed-model ANOVA and time to reaching Cmax (Tmax) by Friedman-test

RESULTS

- In total 26 individuals (12 males, mean [SD] age 62.0 [8.3] years, baseline HbA1c 58 [12] mmol/mol /7.5 [1.1] %, eGFR 96.6 [25.7] ml/min/1.73m^2, BMI 29.2 [4.8] kg/m^2) completed both sequences of this cross over study, of which blood samples were available for BCAA analysis in 25 .

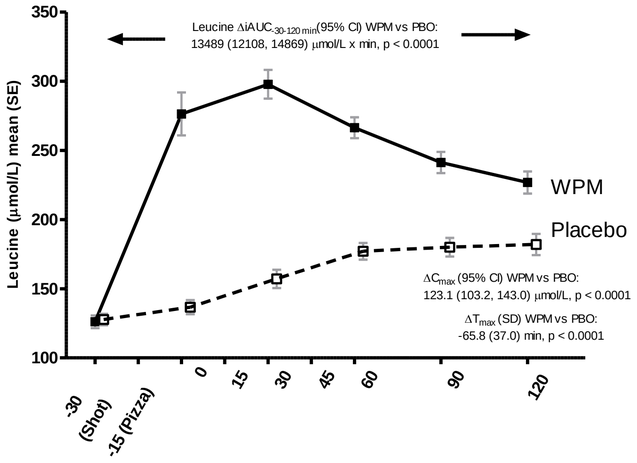
	Mean (SD), or n (%)
Age, years	62.0 (8.3)
Weight, kg	82.9 (15.0)
Body Mass Index, kg/m^2	29.2 (4.8)
Waist circumference, cm	101.3 (12.7)
HbA1c, %	7.5* (1.1)
Fasting plasma glucose, mg/dL	139.9** (42.9)
Total cholesterol, mg/dL	180.4*** (50.0)
Triglycerides, mg/dL	159**** (62)
Systolic/diastolic blood pressure, mmHg	129 (12)/77 (9)
eGFR (MDRD-formula), mL/min/1.73m^2	99.1 (24.7)
Medications	
Metformin	19 (73%)
Glimepiride	1 (4%)
Statins	8 (31%)

Valine trajectory: WPM vs PBO

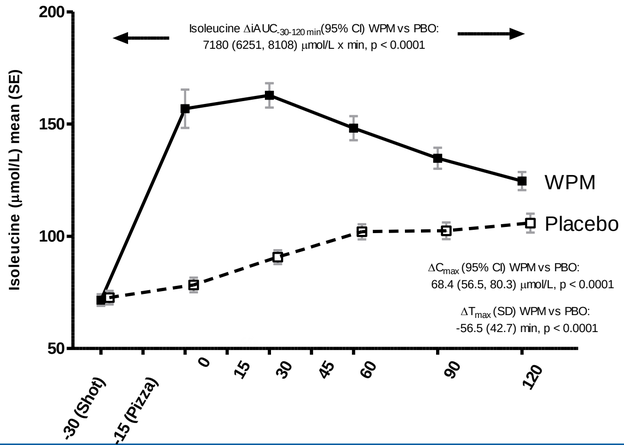


RESULTS (CONT.)

Leucine trajectory: WPM vs PBO



Isoleucine trajectory: WPM vs PBO



LIMITATIONS

- Single center study
- Single-dose experiment
- Limited number of participants
- Post-hoc analysis

DISCUSSIONS AND CONCLUSION

- Compared to PBO, a low dose, low caloric WPM pre-meal drink 15 min before a pizza meal, significantly reduced the early glycemic burden and significantly augmented the GLP-1 response
- The 10g WPM as a pre-meal drink, induced a rapid plasma increase, and high bioavailibilty, of BCAAs in people with T2D
- The rapid BCAA availability might be a likely factor for the metabolic modulatory effects observed with WPM.
- Longer term studies are needed to understand the full translational metabolic impact of this novel WPM formulation

Potential conflict of interests and acknowledgements

Author	Conflicts of interest
Ian J Neeland, MD	Received consulting fee from NHSc and Boehringer Ingelheim
Bo Ahrén, MD	Recevied speaker honoraria from NHSc
John Corthesy	Employment Societe de Produits Nestlé
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Maximilian von Eynatten, MD	Employment NHSc
Odd Erik Johansen, MD, PhD	Employment NHSc

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