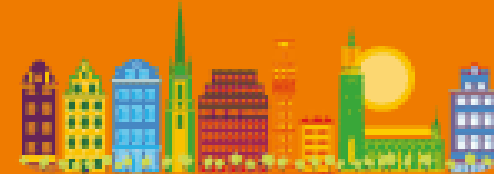


Pre-meal low-dose whey protein microgel increases bioavailability of branched chain amino acids in people with type 2 diabetes: a randomised, PBO-controlled crossover study

Odd Erik Johansen, Bo Ahrén, John Corthesy, Yohan Grzywinski, Zoltan Magos, Maximilian von Eynatten, Ian J Neeland



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Short Oral Discussion Event A, Sept 20 11:45-12:45
SO 37 Dietary and nutritional interventions

Abstract presentation number 541

Disclosures, Author Information, and Acknowledgement



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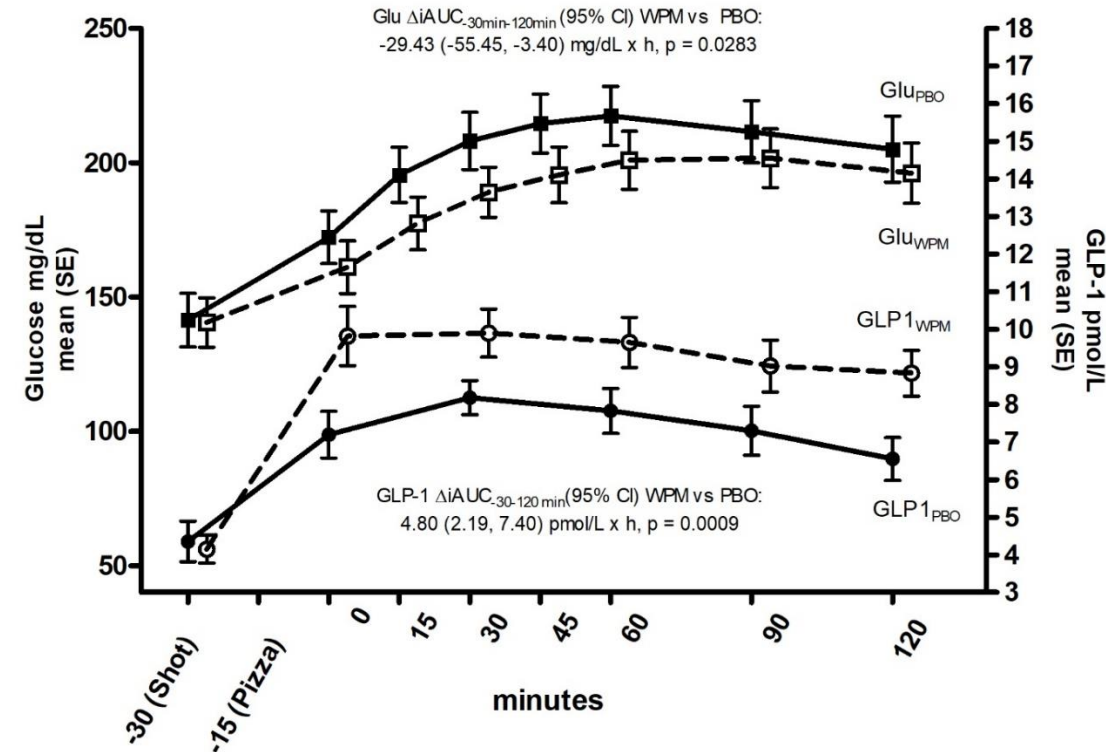
Author	Institution	Conflicts of interest
Odd Erik Johansen, MD, PhD	Nestlé Health Science, Switzerland	Employment NHSc
Bo Ahrén, MD	Lund University, Sweden	Received speaker honoraria from NHSc
Zoltan Magos	Aimmune, UK	Employment Aimmune, a NHSc company
Yohan Grzywinski	Societe de Produits Nestlé	Employment Societe de Produits Nestlé
John Corthesy	Societe de Produits Nestlé	Employment Societe de Produits Nestlé
Maximillian von Eynatten, MD	Nestlé Health Science, Switzerland	Employment NHSc
Ian J Neeland, MD	University Hospitals Cleveland Medical Center; Case Western Reserve University School of Medicine, Cleveland, USA	Received consulting fee from NHSc and Boehringer Ingelheim

- The study was funded by Nestlé Health Science (NHSc)
- We are indebted to the study participants for their commitment to following the trial protocol

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 amino acids, including BCAA, and peptides that can stimulate insulin secretion, but their routine use has been limited by requiring a high dose, and consumption well in advance of a meal
- New micelle-technology [whey protein microgel - 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 minutes ahead of a pizzameal significantly altered the early postprandial glucose trajectory and reduced the 2h incremental area under the curve by 22% while at the same time increased the total GLP-1 response by 66% (Figure)



Johansen OE, et al. EASD 2021, OP 112

WPM has highly concentrated, bioavailable BCAAs

British Journal of Nutrition (2010), 104, 1241–1248
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doi:10.1017/S0007114510001911

The acute effects of four protein meals on insulin, glucose, appetite and energy intake in lean men

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Key finding:

Of four different protein sources, namely whey, tuna, turkey and egg albumin, the whey protein meal has the highest % (w/w) of BCAAs and produced a greater insulin response, reduced appetite and decreased ad libitum energy intake at a subsequent meal compared with the other protein meals

Am J Physiol Endocrinol Metab 320: E874–E885, 2021.
First published March 1, 2021; doi:10.1152/ajpendo.00026.2021



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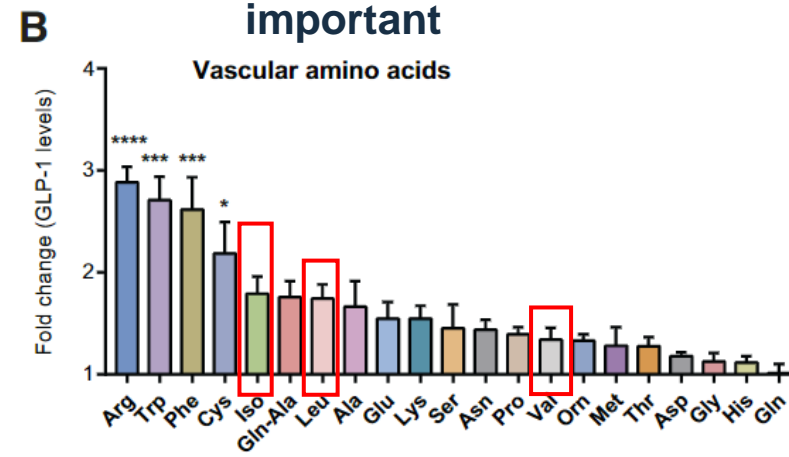
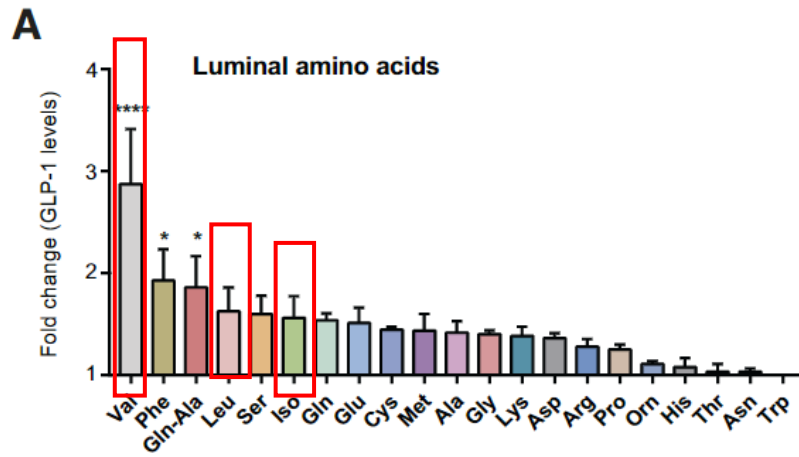
RESEARCH ARTICLE

Deciphering the Contribution of the Gastrointestinal Tract on Glucose, Lipid, and Energy Metabolism

Amino acids differ in their capacity to stimulate GLP-1 release from the perfused rat small intestine and stimulate secretion by different sensing mechanisms

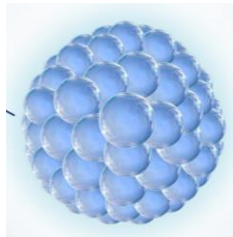
Some AAs stimulated secretion only from the intestinal lumen, whereas other AAs exclusively stimulated secretion from the vascular side, indicating that AA-stimulated GLP-1 secretion involves both apical and basolateral (postabsorptive) sensing mechanisms. **The BCAA has predominantly a “flushing” effect, suggesting that their immediate bioavailability is important**

Modvig, .. Holst et al.



Objectives

- To assess the effects of whey protein microgel (WPM) on free plasma branched chain amino acids (BCAA) trajectories



Schematic illustration of the highly concentrated WPM structure

Methods

- This crossover study in drug-naïve or metformin-treated T2D with overweight or obesity, studied the effects of 10g WP (40 kcal) prepared as WPM, or placebo (PBO, 0 kcal [water – for volume equivalence]), provided as a 125mL shot 15 min ahead of a 250 g pizza meal (622kcal [29.0g protein, 22.6 g fat, 72.6 g carbohydrates]).
- PP BCAA trajectories were evaluated in a post-hoc analysis in frequently drawn blood-samples over a 2h period.
- The differences between WPM and PBO were assessed by comparing change in iAUC as well as by comparing maximum concentrations reached (C_{max}) by mixed-model ANOVA and time to reaching C_{max} (T_{max}) by Friedman-test
- NCT04639726

Baseline characteristics of the participants



	n (%)
Sex	
Female	14 (54%)
Male	12 (46%)
Ethnicity	
Hispanic or Latino	9 (34.6%)
Not hispanic or Latino	17 (65.4%)
Race	
Asian	3 (11.5%)
Black or African American	4 (15.4%)
White	19 (73.1%)

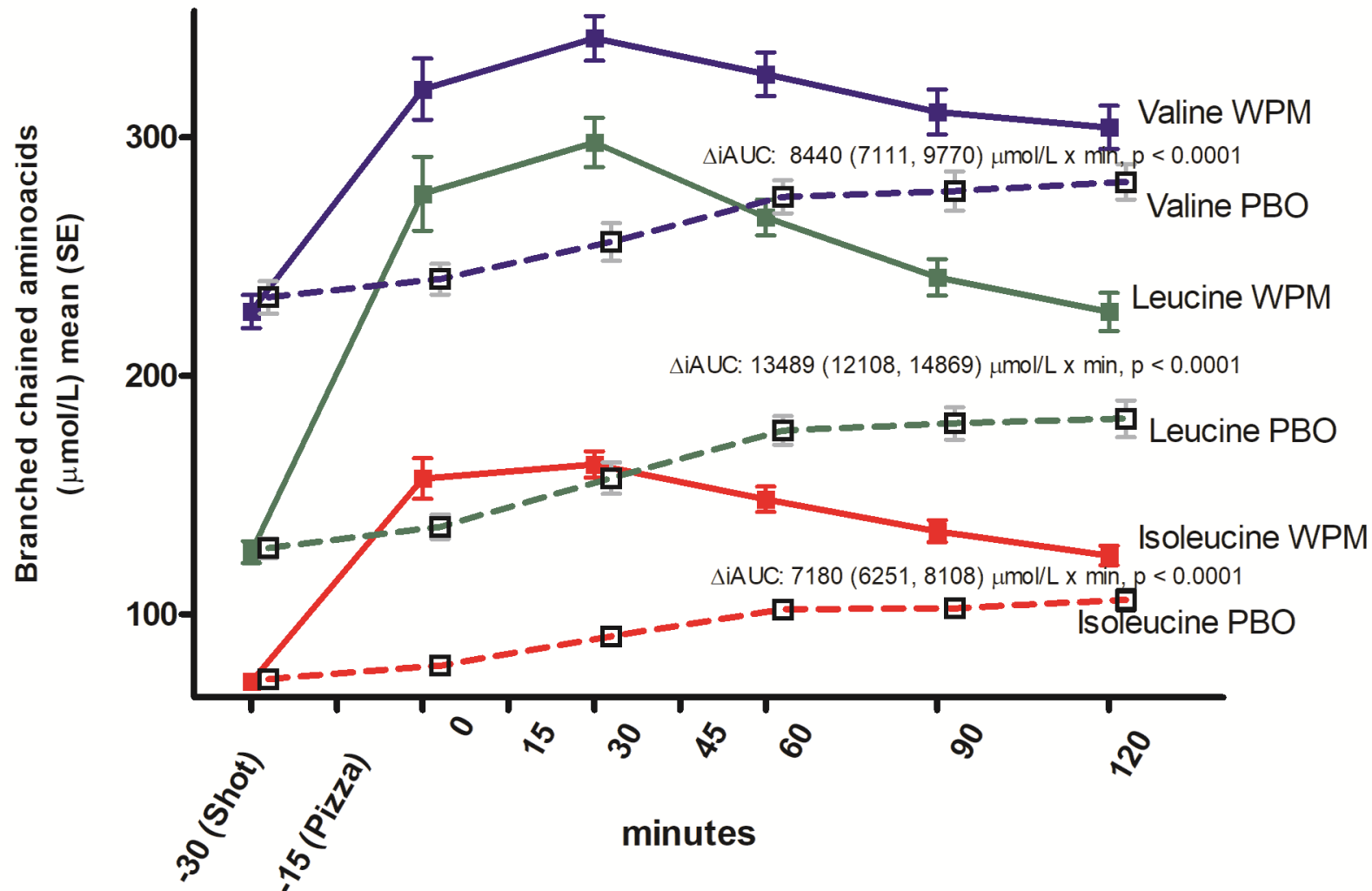
Blood samples were available for BCAA analysis in n=25

	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%)

*58 mmol/mol; Old HbA1c = 0,0915 New + 2,15%
 **7.8 mmol/L; mg/dL to mmol/L glucose: multiply with 0.0555
 ***4.7 mmol/L; multiply by 0.02586
 ****1.8 mmol/L; multiply by 0.01129

BCAA trajectories

WPM induced a rapid plasma increase of BCAA and increased their bioavailability by 194 to 267%



Limitations

- Single center study
- Acute study
- Limited number of participants
- Post-hoc analysis

Conclusion

- Compared to PBO, 10g WPM taken 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 bioavailability, 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