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### Dileucine-enriched essential amino acids support greater whole-body anabolism than branched chain amino acids and collagen hydrolysate after resistance exercise in recreationally active adults Jonathan A. Aguilera<sup>1</sup>, Matthew J. Lees<sup>1</sup>, Cassidy T. Tinline-Goodfellow<sup>1</sup>, Megha Sharma<sup>2</sup>, Raza Bashir<sup>2</sup>, Sidney Abou Sawan<sup>2</sup>, Daniel R. Moore<sup>1</sup> 1 Faculty of Kinesiology and Physical Education, University of Toronto; 2 lovate Health Sciences International Inc, Oakville, ON L6M0H4 Canada

## Abstract

Essential amino acid ingestion after resistance exercise stimulates muscle protein synthesis and whole-body anabolism (i.e., growth). Previous work has demonstrated that ingestion of 2g of dileucine is more effective at stimulating myofibrillar protein synthesis compared to 2g of leucine in young men at rest. We aimed to determine the effect of a dileucine-containing essential amino acid formula (DIEAA; 2g dileucine, 1g leucine) on the anabolic response after resistance exercise in young recreationally active adults when compared with ingesting branched chain amino acids (BCAA; 3g leucine, 1.5g isoleucine, 1.5g valine) or isonitrogenous collagen hydrolysate (COL). In a randomized, double-blind, crossover design, 12 healthy adults (8M, 4F, age 24 ± 3 y) performed a 60 min bout of whole-body resistance exercise after which they ingested DIEAA, BCAA, or COL protein beverages with 100 mg L-[1-<sup>13</sup>C]leucine. Total exogenous leucine retention (as an estimate of whole-body anabolism) was assessed over the 6 h postprandial period by determining total leucine oxidation from <sup>13</sup>CO<sub>2</sub> enrichment in repeated breath samples. Urinary 3methylhistidine:creatinine ratio (3MH:Cr, estimate of skeletal muscle myofibrillar protein breakdown (MPB)) was also assessed over the 6 h postprandial period. Total exogenous leucine retention was greater in DIEAA compared to BCAA by 161% with both DIEAA and BCAA greater than COL by 852% and 530%, respectively (all p<0.01). There were no differences (p=0.58) in 3MH:Cr between conditions. Dileucine-enriched essential amino acids supported greater whole-body anabolism than BCAA or COL after resistance exercise independent of any attenuation in estimates of MPB in healthy young adults. In conclusion, our research provides the first insights into enriching dileucine peptides in conjunction with essential amino acids to enhance post-exercise anabolism.

### Introduction

Food-borne peptides (di- and tri-peptides) and their intact absorption<sup>1</sup> into circulation can regulate skeletal muscle metabolism<sup>2</sup>.

The intestinal absorption of intact dipeptides is up to 185% greater than that of free-form amino  $acids^3$ .

Previous work has demonstrated that the ingestion of 2g of dileucine (leucine-leucine dipeptide) was more effective at stimulating myofibrillar protein synthesis compared to 2g of leucine in young men at rest<sup>4</sup>.

Following resistance exercise, the ingestion of essential amino acids can enhance wholebody anabolism and attenuate markers of myofibrillar proteolysis<sup>5</sup>.

Thus, it seems plausible that the ingestion of dileucine following resistance exercise could enhance or augment the whole-body anabolic response, although evidence to support this hypothesis is lacking.

We aimed to determine the effect of a dileucine-containing essential amino acid formula (DIEAA) on the anabolic response after resistance exercise when compared with ingesting branched chain amino acids (BCAA) or isonitrogenous collagen hydrolysate (COL).

References

12 healthy adults (8M, 4F, age 24  $\pm$  3 y, 72.0  $\pm$  17.5 kg, BMI 24.1  $\pm$  3.8 kg/m<sup>2</sup>) participated in a randomized, doubleblind, crossover study design.

- and 4) leg extension.
- 1.5g valine), or COL protein beverages with 100 mg L-[1-<sup>13</sup>C]leucine.
- of skeletal muscle myofibrillar protein breakdown.
- intake and total leucine oxidation.



Figure 1: Time course of exogenous leucine oxidation (A) and total exogenous leucine oxidation expressed as an absolute amount (B) and as a percentage of total leucine intake (C). Data are presented as mean  $\pm$  SD. Conditions that do not share a letter are significantly different (P < 0.001). \* COL different from BCAA, # COL different from DIEAA, † BCAA different from DILEU (all P < 0.05).

#### Whole-body muscle protein breakdown was not attenuated by the provision of essential amino acids



**Figure 3:** 3-methylhistidine:creatinine ratio. Data are mean  $\pm$  SD. Main effect of P = 0.584

## Methods

Participants completed a 60 min bout of whole-body resistance exercise (4 x 8-10, 75% 1RM) that involved the following 4 exercises: 1) bench press and cable row superset, 2) shoulder press and lat pulldown superset, 3) leg press,

• After resistance exercise, participants ingested DIEAA (2g dileucine, 1g leucine), BCAA (3g leucine, 1.5g isoleucine,

Breath samples were collected to determine  ${}^{13}CO_2$  enrichment and total leucine oxidation.

• Urinary 3-methylhistidine(3MH):creatinine ratio was assessed over the 6 h postprandial period to provide an estimate Beverage

• Total leucine retention (estimate of whole-body anabolism) was determined by the difference between total leucine

### Results

Greater total exogenous leucine oxidation in DIEAA compared to BCAA and COL



Dileucine-enriched essential amino acids supported greater whole-body anabolism than BCAA or COL after resistance exercise independent of any attenuation in estimates of MPB in healthy young adults.

These findings suggest that dileucine is an efficient way of providing leucine to the body for supporting whole-body growth in individuals performing resistance exercise.

Our research provides the first insights regarding the enrichment of an essential amino acid mixture with dileucine peptides to enhance post-exercise anabolism.



Greater total leucine retention (whole-body protein synthesis) in DIEAA compared to BCAA and COL

**Figure 2:** Total exogenous leucine oxidation. Data are presented as mean ± SD. Conditions that do not share a letter are significantly different (P < 0.001).

# Conclusions



<sup>&</sup>lt;sup>3</sup> Adibi, S. A., J. Clin. Investig., 50, 2266-2275, 1971

<sup>&</sup>lt;sup>5</sup> Waskiw-Ford, M., *Nutrients*, 14, 3532, 2022