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**Effect of a Probiotic Supplement on Insulin Sensitivity and
Skeletal Muscle Substrate Oxidation during High Fat Feeding.**

Kristin Linnea Osterberg

Dissertation submitted to the faculty of Virginia Polytechnic Institute and State University in
partial fulfillment of the requirements for the degree of

Doctor of Philosophy

In

Human Nutrition, Foods and Exercise

Kevin P. Davy, Chair

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Keywords: Probiotic, High Fat Diet, Insulin Resistance, Substrate Oxidation

Effect of a Probiotic Supplement on Insulin Sensitivity and Skeletal Muscle Substrate Oxidation during High Fat Feeding.

Kristin Linnea Osterberg

Background: Modifying the gut microbiota through the administration of probiotics during high fat feeding has been shown to attenuate weight gain and body fat accretion while improving insulin sensitivity in animal models.

Objective: Our objective was to determine the effects of the probiotic VSL#3 on body weight and composition, skeletal muscle substrate oxidation, and insulin sensitivity and during 4 weeks of high-fat, hypercaloric feeding. We hypothesized that the probiotic would attenuate the body weight and fat gain and adverse changes in insulin sensitivity and substrate oxidation following high fat, hypercaloric feeding in young, non-obese males.

Methods: Twenty non-obese males (18-30 y) volunteered to participate in the present study. Following a 2-week eucaloric control diet, subjects underwent a dual x-ray absorptiometry (DXA) to determine body composition, an intravenous glucose tolerance test (IVGTT) to determine insulin sensitivity, a skeletal muscle biopsy for measurement of substrate oxidation. Serum endotoxin was also measured. Subsequently, subjects were randomized to receive either VSL#3 (2 satchets) or placebo during 4 weeks of consuming a high fat (55% fat), hypercaloric diet (+1,000 kcal/day). Macronutrient composition of the high fat diet was 55% fat, 30% carbohydrate, and 15% protein.

Results: There were no differences between the groups in subject characteristics or in the dependent variables at baseline. Body weight and fat mass increased less ($P < 0.045$) following the high fat diet with VSL#3 compared to placebo. Insulin sensitivity (and other IVGTT variables) and both glucose and fat oxidation did not change significantly with time or VSL#3 treatment. Serum endotoxin concentration was not different between groups following the high-fat diet.

Conclusions: VSL#3, a multi-strain probiotic, attenuated body weight and fat gain following a 4-week high fat, hypercaloric diet compared with a placebo. There were no differences between the VSL and control in circulating endotoxin, insulin sensitivity (and other IVGTT variables) or in skeletal muscle substrate oxidation.

Key words: Probiotic, gut microbiota, high-fat feeding, endotoxin