Physical Activity and the Metabolic Effects of S-equol in Mice Fed an Obesogenic Diet

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Introduction

In the U.S. and 35 other recorded countries, obesity rates continue to rise dramatically, with the U.S., Mexico, and England projected for 47%, 39%, and 35% obesity by 2030 (1). It has become imperative to find options to combat obesity, and the metabolite S-equol could be an adjuvant treatment. In 25% of Western individuals and 80% of Asian individuals, soy is naturally converted by gut bacteria to a metabolite called S-equol (2). S-equol has shown beneficial effects in those who produce it—like reduced prostate disease in men (3) and alleviation of menopausal symptoms in women (4). While select research has been conducted on S-equol, sex effects, exogenous dosing, and ability to negate obesogenic diet and promote activity have not been addressed. This research bridges these gaps by comparing the metabolic effects of S-equol treated mice to control mice.

Hypothesis

Mice treated with S-equol will demonstrate metabolic resistance to an obesogenic diet, as evidenced by increased voluntary physical activity, lower fat content, and faster glucose clearing times.

Methods

28 5-week-old C57 mice were placed on a high fat diet (HFD) and assigned four groups: 7 females on S-equol, 7 females on control, 7 males on S-equol, and 7 males on control. The control solution contained 2.5% DMSO/0.5% CMC while the treatment solution contained 10 mg/kg body weight S-equol in 2.5% DMSO/0.5% CMC.

All 28 mice were dosed daily with respective solutions for two months. Over the course of one month, the following experiments were conducted and samples collected: Promethion Indirect Calorimetry Unit (**Fig 1.**), Echo MRI (**Fig 2.**), glucose tolerance tests (**Fig 3.**), tissue collection, and plasma samples (**Fig 4.**).

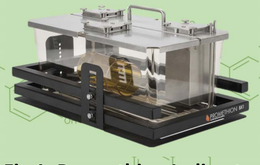


Fig 1. Promethion Indirect Calorimetry Unit: measures activity, sleep, RQ value, water and food consumption, and several other variables.

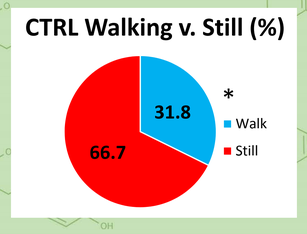
Fig 2. Echo MRI: measures fat and water content.

Fig 3. Glucose Tolerance Test: tests body's ability to clear glucose.

Fig 4. Plasma samples: including leptin, adiponectin, insulin, glucose, and corticosterone.

Pictures courtesy of Sable Systems, EchoMRI, AlphaTrak2, and MedSupply Partners, respectively.

S-equol may lead to negative metabolic outcomes.



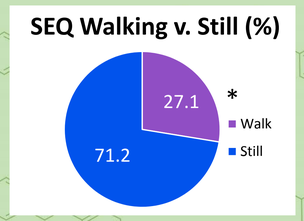


Fig 5. The control (CTRL) group spent 31.8% of time in the Indirect Calorimetry Unit walking and 66.7% of time still. The treatment group (S-equol, SEQ) spent 27.1% of time walking and 71.2% of time still. *p<.0001 for each comparison. **Not pictured**: The control group spent 60.6% of time sleeping while the treatment group spent 65.6% of time sleeping.

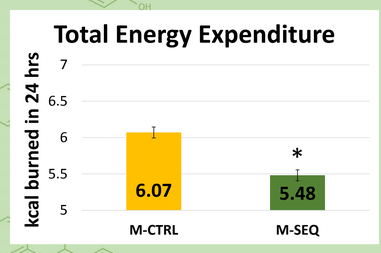


Fig 6. The average 24 hour energy expenditure of male control (M-CTRL) was 6.07 kcal, while that of male S-equol (M-SEQ) was 5.48 kcal. SEM=.0755. *p<.0001.

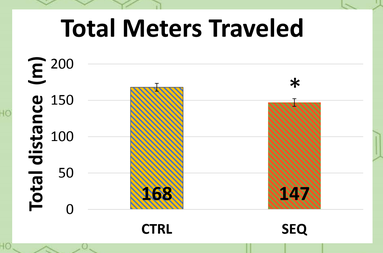


Fig 7. For the two days spent in the Indirect Calorimetry Unit, the control group walked 168 meters while the treatment group walked 147 meters. SEM=5.3289. *p=.0061.

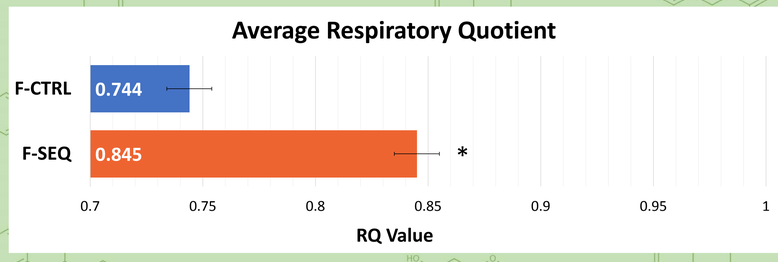


Fig 8. The average RQ value is the ratio of the volume of CO_2 exhaled to O_2 inhaled, CO_2/O_2. An RQ value approaching 0.7 indicates that the organism is burning fats, while an RQ value approaching 1.0 indicates the burning of carbohydrates. Female control v. treatment showed a significant difference, with SEM=.0100 and *p<.0001.

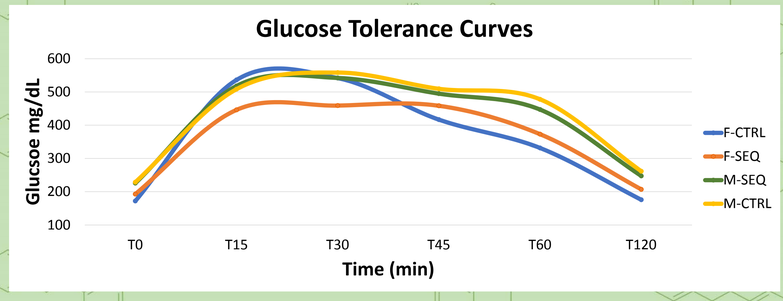


Fig 9. Glucose tolerance tests measure an individual's ability to clear blood glucose after injection into the peritoneal cavity. None of the results were significant, with p>0.05 for each data point.

Conclusions

Current data collected indicates that exogenous dosing of S-equol may lead to detrimental metabolic effects.

- In the home cage setting, the control group exhibited significantly more activity than the S-equol treatment group.
- Surprisingly, control males burn more calories in a day than those receiving S-equol treatment solution.
- Control females burn more fats than carbohydrates, while S-equol treated females burn more carbohydrates than fats.
- Taken together, the combined results suggest that mice fed a HFD and provided S-equol demonstrate negative metabolic health outcomes.

Future Direction

- Serum chemistry and metabolic hormonal measurements are currently pending.
- As S-equol is naturally produced by some gut flora, it would be of interest to determine how this nutrient supplement effects the gut microflora (see **Fig 10.**).
- Gene expression studies will examine how S-equol treatment affects the nucleus accumbens, the brain region guiding voluntary physical activity (see **Fig 11.**), and white adipose tissue.

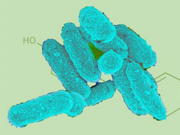


Fig 10. Gut Bacteria. How does exogenous dosing of S-equol influence the gut microbiota?

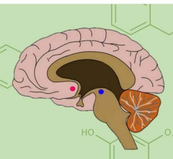


Fig 11. Nucleus Accumbens. Does S-equol alter the structure of the nucleus accumbens?

Pictures courtesy of The Hearing Review and neuroscientificallychallenged.com, respectively.

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