

### **6-amino-6-deoxy paramylon improved obesity and glucose metabolism in a diet-induced obesity mouse model**

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**Background and aims:** Obesity and type 2 diabetes are preventable causes of death. Bile acid binding resins are beneficial for obesity and diabetes, but they are more likely to accompany abdominal distention and constipation. These side effects can be prevented by using dietary fiber.  $\beta$ -glucan is one of the dietary fiber and is reported to improve obesity and glucose metabolism. Barley or oat  $\beta$ -glucan increases fecal output of fat and bile acids synthesis from cholesterol in the liver. Paramylon is one of the component of green algae, Euglena, and consists of  $\beta$ -glucan. Besides barley or oat  $\beta$ -glucan, paramylon is reported to have no effect on hyperglycemia in diabetic rats. Here we generate cationized 6-amino-6-deoxy paramylon, which is just like bile acid binding resins. The effect of 6-amino-6-deoxy paramylon on obesity and glucose metabolism were examined in a diet-induced obesity mouse model.

**Materials and methods:** As an in vitro experiment, bile acids were incubated with 6-amino-6-deoxy paramylon in a fed state simulated human intestinal fluid. After that, the adsorption rate of bile acid was measured. Furthermore, in an experiment using animals, male C57BL/6J mice were fed high-fat (HF) diets supplemented with 6-amino-6-deoxy paramylon for 5 weeks. Body weight, blood sugar, serum LDL cholesterol, fecal bile acid composition and fecal lipid content were assessed. Hepatic small heterodimer partner (SHP) and cholesterol 7 alpha-hydroxylase (CYP7A1) gene expression levels were also analyzed to investigate the effect of 6-amino-6-deoxy paramylon on bile acids synthesis.

**Results:** Although paramylon barely absorbed bile acids, 6-amino-6-deoxy paramylon absorbed effectively in a simulated intestinal fluid. In mice, supplementation of 1% or 2% 6-amino-6-deoxy paramylon in a HF diet led to significant weight gain reduction (HF, 1%, 2%; +7.72 + 3.1, +4.16 + 1.4, +0.15 + 0.86 g). Significant decreases in concentrations of blood sugar (HF, 1%, 2%; 161 + 42, 138 + 23, 95 + 41 mg/dl) and serum LDL cholesterol (HF, 1%, 2%; 16.0 + 1.2, 9.4 + 2.1, 8.8 + 2.5 mg/dl) were shown. Strongly positive staining for Sudan IV in fecal smears indicated altered fat absorption when 6-amino-6-deoxy paramylon was supplemented in the HF diet. The composition of fecal bile acids were completely different, secondary bile acids were almost absent and primary bile acids like tauro- $\beta$ muricholic acids were dominated in feces of mice supplemented with 6-amino-6-deoxy paramylon. Moreover, decreased levels of SHP mRNA and increased levels of CYP7A1 mRNA were shown in the liver of mice supplemented with 6-amino-6-deoxy paramylon. 6-amino-6-deoxy paramylon had no effect on the food consumption and histology of digestive systems.

**Conclusion:** 6-amino-6-deoxy paramylon increased fecal output of fat and increases bile acids synthesis from cholesterol in the liver, thus improved obesity and glucose metabolism in a diet-induced obesity mouse model.

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