

# Supplementation of geranylgeraniol and tocotrienols to high-fat diet shifts the gut microbiome composition and function in type 2 diabetic mice

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## Abstract

**INTRODUCTION** In recent years, characterization of gut microbiota composition and function were linked to the progression of type 2 diabetes mellitus. Recent evidence showed that Geranylgeraniol, an isoprenoid found in fruits, vegetables, and grains, improves glucose homeostasis. Similarly, Tocotrienol, a subfamily of vitamin E, also contains anti-diabetic properties. In this study, we examined the combined effect of geranylgeraniol and tocotrienols on the composition and function of gut microbiome in obese male mice. **METHOD** Forty male C57BL/6J mice were assigned to 4 groups in a factorial design as follows: high-fat diet (HFD) (control group), HFD+geranylgeraniol [400 mg/kg diet] (GG group), HFD+tocotrienol [400 mg/kg diet] (TT group), and HFD+geranylgeraniol+tocotrienol (G+T group) for 14 weeks. 16S rRNA gene sequencing was done from cecal samples and microbiome and data analysis was performed with QIIME2 and PICRUST2. **RESULTS** Across all groups, the most abundant phyla were Verrucomicrobia, Firmicutes, Bacteroidetes, and Actinobacteria. There was no difference in alpha diversity among different groups. Different treatments influenced the relative abundance of certain bacteria. In the Bacteroidetes phylum, the relative abundance of family S24-7 increased in the TT group only. In the Firmicutes phylum, the relative abundance of family Lachnospiraceae was reduced upon the supplementation of geranylgeraniol or tocotrienols; individually or in combination. In Verrucomicrobia phylum, *Akkermansia muciniphila* relative abundance was reduced in the TT group but increased in the G+T group. The results of functional profiling of the gut microbiome revealed that geranylgeraniol supplementation caused an increase in the proportion of biosynthetic pathways related to purine, pyrimidine, and inosine-5-phosphate and hexitol fermentation, and a decrease in the proportion of pathways involved in the biosynthesis of isoleucine, valine,

## Methods

## Results

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