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File: ■ Garlic (*Allium sativum*, Amaryllidaceae)
■ Hypertension
■ Gut Microbiota
■ Inflammation

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RE: Aged Garlic Extract Reduces Blood Pressure and Improves Gut Microbiota in Patients with Uncontrolled Hypertension

Ried K, Travica N, Sali A. The effect of Kyolic Aged Garlic Extract on gut microbiota, inflammation, and cardiovascular markers in hypertensives: the GarGIC Trial. *Front Nutr*. December 11, 2018;5:122. doi: 10.3389/fnut.2018.00122.

Garlic (*Allium sativum*, Amaryllidaceae) bulb extracts have been shown to reduce central blood pressure (BP), pulse wave velocity (PWV), pulse pressure, and arterial stiffness, which are predictors of cardiovascular disease. Hypertension has been linked to gut microbial dysbiosis, including a decrease in gut microbial richness and diversity and a significant increase in the *Firmicutes*-to-*Bacteroidetes* ratio (F/B ratio). In turn, gut microbial dysbiosis has been associated with increased inflammatory status, chronic inflammatory diseases, and increased risk for cardiovascular events. In addition to reducing blood pressure, the prebiotic properties of garlic may help modulate the gut microbiota and protect against intestinal inflammation. The randomized, controlled, double-blind GarGIC (GARlic, Gut microbiota, Inflammation, and Cardiovascular markers) trial evaluated the effect of Kyolic Aged Garlic Extract (Wakunaga of America Co., Ltd.; Mission Viejo, California) on BP, PWV, arterial stiffness, inflammatory markers, and gut microbiota.

The GarGIC trial was conducted at the National Institute of Integrative Medicine (NIIM) in Melbourne, Australia, from May 2016 to October 2017. Adults with uncontrolled hypertension [systolic BP (SBP) ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg] who had been on blood pressure medication for at least two months or who were not taking any blood pressure medication were recruited through the NIIM clinic newsletter and website, and locally distributed flyers. The exclusion criteria were unstable medical conditions or serious illness; pregnancy; severe hypertension (mean sitting SBP ≥180 mm Hg and DBP ≥110 mm Hg); surgery planned in the next three to four months; history of intestinal surgery, inflammatory bowel disease, celiac disease, lactose intolerance, chronic pancreatitis, or diagnosed malabsorption disorder; antibiotic treatment within two months of study enrollment; and taking prescribed anti-inflammatory agents, glucocorticoids, or other immune regulating prescription medication. Potential

participants were advised to cease any probiotics or garlic supplementation at least two months prior to enrollment.

Participants (n=52, aged 62 ± 10 years) were randomly assigned to take two capsules daily of either Kyolic Aged Garlic Extract or placebo (inert microcrystalline cellulose) for 12 weeks. Each Kyolic garlic capsule contained 1.2 g of aged garlic extract powder and 1.2 mg *S*-allylcysteine.

Primary outcome measures were SBP and DBP at weeks 4, 8, and 12 compared to baseline. Central hemodynamic measures (central blood pressure, PWV, pulse pressure, and arterial stiffness) were assessed at baseline and at weeks 4, 8, and 12. Fasting blood draws and stool samples were collected at baseline and after 12 weeks. Changes in serum levels of the inflammation markers tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), and gut microbiota richness, diversity, and F/B ratios were determined.

Baseline characteristics did not significantly differ between the two groups except for SBP, which was significantly higher in the garlic group (P=0.05). Of the 49 participants who completed the study, 45% were males. Sixty percent had a family history of cardiovascular events and 63% took BP medication. Three patients in the garlic group withdrew due to illness unrelated to the intervention.

Significant decreases were observed in DBP (P=0.02) and SBP (P=0.008) in the garlic group compared with the placebo group. Central SBP (P=0.01), pulse pressure (P=0.008), central pulse pressure (P=0.04), mean arterial pressure (P=0.05), and age- and gender-adjusted PWV (P=0.046) significantly improved in the garlic group compared with the placebo group. Garlic supplementation improved gut microbiota as shown by higher microbial richness (a marked increase in *Lactobacillus* and *Clostridia* species) and a small increase in microbial diversity compared with the placebo group. The F/B ratio decreased slightly in the garlic group and increased slightly in the placebo group. Between-group differences in changes in TNF-α and IL-6 levels were not significant. No adverse effects were reported.

The authors conclude that Kyolic Aged Garlic Extract "is effective in reducing blood pressure in patients with uncontrolled hypertension, and has the potential to improve arterial stiffness, inflammation, and gut microbial profile." Limitations of this study include the small sample size and short duration. Larger, longer duration trials are needed to further evaluate the effects of aged garlic extract on gut microbiota, inflammation, and immunity.

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—Shari Henson

Referenced article can be accessed at https://www.frontiersin.org/articles/10.3389/fnut.2018.00122/full.