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File: ■ Garlic (*Allium sativum*, Amaryllidaceae)

■ Hypertension

■ Hypercholesterolemia

■ Immune Modulation

■ Meta-analysis

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RE: Meta-analysis Shows Garlic Supplements Effective in Lowering Blood Pressure in Patients with Hypertension, Stimulating the Immune System, and Reducing Serum Cholesterol

Ried K. Garlic lowers blood pressure in hypertensive individuals, regulates serum cholesterol, and stimulates immunity: An updated meta-analysis and review. *J Nutr.* February 2016;146(2):389S-396S.

Cardiovascular disease is a major cause of death worldwide. High blood pressure (hypertension) is one of the strongest risk factors for cardiovascular illnesses, but antihypertensive medications have been associated with a wide range of side effects. High levels of serum cholesterol and low-density lipoprotein (LDL) cholesterol also are associated with increased risk of cardiovascular disease. Statins are commonly used to lower lipid and serum cholesterol levels, but in addition to side effects, there is growing evidence showing that statins may interfere with essential biochemical pathways.

As an herbal alternative, garlic (*Allium sativum*, Amaryllidaceae) has been linked to improved cardiovascular health with minimal side effects. This author and colleagues previously reviewed and conducted meta-analyses of the effects of garlic on blood pressure¹ and serum lipids.² Garlic showed moderate but significant reductions in blood pressure and cholesterol, with few adverse side effects. In this publication, an updated meta-analysis of garlic's effects on blood pressure is presented, as well as comments on published information regarding effects on cholesterol and immune activity. Traditionally, garlic has been used as an antibiotic, immune modulator, and general tonic. Cell culture and in vitro studies show that garlic has antibacterial, antiviral, antifungal, and antiparasitic properties. It inhibits bacterial biofilms from forming on burn wounds and supports healthy bacterial flora. Studies have shown that garlic also benefits the immune system by reducing C-reactive protein, interleukins, and other inflammatory cytokines associated with cardiovascular disease.

To update the original garlic-blood pressure meta-analysis,¹ the Medline database was searched for clinical trials published between January 2008 and December 2013 using

the search terms "garlic," "hypertension," and "blood pressure." The author identified five new, randomized, controlled, clinical trials where a garlic supplement was compared to a placebo and where mean systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) were reported. In four of these, mean SBP in the participants or a subgroup of participants was high enough to constitute hypertension. The author of this review was a co-author for two of the newly included trials.

An additional 15 trials were obtained from three sources. The primary source was the author's original 2008 meta-analysis,¹ which searched Medline and Embase from 1955 through October 2007 (n=10). The remaining five trials were included from clinical trial reviews and meta-analyses by Silagy and Neil³ and Reinhart et al.⁴ Two of the new trials utilized four-group parallel trials with active garlic groups of different dosages; the analysis included only one active group (compared with placebo) from each of these two trials. [Note: For one, the dosage of the included group does not correspond to any of those listed in Table 1, resulting in uncertainty as to what data were analyzed.] In total, 25 trial arms and >900 subjects from 20 trials were stated to have been analyzed.

Supplements used in the trials included garlic powder (n=13), aged garlic extract (n=5), garlic oil (n=1), and garlic powder enriched with egg yolk (n=1). Garlic powder supplements were either Kwai[®] (MCM Klosterfrau Healthcare GmbH; Cologne, Germany), given in doses containing 7.8 to 11.7 mg alliin, or in two studies, Allicor[®] (INAT-Farma; Moscow, Russia), given in doses containing 7.8 mg (or in one arm, possibly not analyzed, 31.2 mg) allicin. The garlic oil tablet was Cardiomax[®] (Seven Seas Ltd; Hull, United Kingdom), with a dosage of 12.3 mg oil. Studies of aged garlic extract tablets used Kyolic[®] (Wakunaga of America, Co., Ltd. [Mission Viejo, California] and Wakunaga Pharmaceutical Co., Ltd. [Hiroshima, Japan]); analyzed trial arms supplied 1.2 mg, 2 mg, 2.4 mg, or 14.7 mg of S-allylcysteine per dose. The garlic powder with egg yolk, Dentou-ninniku-ranwo (Kenkoukazoku Inc.; Kagoshima, Japan), contained 188 mg of garlic per dose.

Overall, there was a significant reduction in the mean SBP and DBP for subjects treated with garlic supplements compared to placebo. For SBP, the mean ($\pm$ standard error [SE]) reduction was 5.1 ± 2.2 mm Hg ($P < 0.001$); and for DBP, the mean reduction was 2.6 ± 1.6 mm Hg ($P < 0.001$). Effects were larger in hypertensive subjects, with mean SBP reduced by 8.6 ± 2.2 mm Hg ($P < 0.001$) and mean DBP reduced by 6.1 ± 1.3 mm Hg ($P < 0.001$). In contrast, the difference between garlic and placebo for prehypertensive or normal baseline subjects was much smaller and not significant. Blood pressure at baseline was found to be strongly related to the effect of garlic on blood pressure reduction.

Garlic is considered to have minimal side effects, primarily odor and mild gastrointestinal discomfort, and is not known to interact with most prescription medications. The author notes, however, that there is a potentially harmful interaction between garlic and the protease inhibitors used in antiretroviral therapy.

The author concludes that garlic improves cardiovascular health by lowering blood pressure. Additionally, she cites evidence that garlic beneficially affects serum cholesterol and the immune system, the latter activity possibly reducing levels of pro-inflammatory molecules. Garlic supplements show great promise for safely reducing the risk of cardiovascular disease.

While the author notes that long-term controlled trials are still needed, especially with regard to morbidity and mortality, this meta-analysis shows that by re-examining trials, patterns emerge that help to focus future clinical trials. The presence of large study effects along with variations in trial durations, supplement type, dosage, etc., are well illustrated and provide the groundwork for increasingly valid clinical studies. [Note: While published in 2016, the original presentation of this study was in 2014. A 2015 meta-analysis further updates this research.^{5]}

The author states no conflict of interest. The author received travel sponsorship from Wakunaga of America Co., Ltd., to attend the 2014 International Garlic Symposium in Dana Point, California. The author also notes that according to the US Code of Federal Regulations (18 U.S.C. § 1734 [2014]), the journal supplement (in which this article appears) must be marked as an advertisement.

—Kathleen Bennett, MS

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The American Botanical Council has chosen not to reprint the original article.

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