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

HC 021746-574

Date: August 15, 2017

RE: Review of Meta-analyses of Clinical Trials of Garlic Emphasizes Evidence for Reductions of Blood Pressure and Total Cholesterol

Schwingshackl L, Missbach B, Hoffmann G. An umbrella review of garlic intake and risk of cardiovascular disease. *Phytomedicine*. October 15, 2016;23(11):1127-1133.

Cardiovascular disease (CVD) causes nearly one-third of global deaths annually, and age-adjusted death rates have increased in recent decades. CVD-related disorders have complex etiologies and share some modifiable risk factors including high cholesterol, high blood pressure (BP), and diabetes type 2 (DT2). Dietary substances such as β-glucans, soy (*Glycine max*, Fabaceae) protein, isoflavones, plant sterols and stanols, and garlic (*Allium sativum*, Amaryllidaceae), which affect those risk factors, are being used to reduce risk of CVD. Garlic's active compounds, including flavonoids, steroid saponins, and organosulfur compounds including allicin, alliin, *S*-allylcysteine, allyl disulfide, and *S*-allyl mercaptocysteine, have been reported to exert antilipidemic, antithrombotic, antihypertensive, antiatherogenic, and antidiabetic effects in vivo. Allicin has been identified, of garlic compounds studied so far, as having the most antioxidative potential, and garlic's antioxidative effects have been identified as one of its main mechanisms of action. Garlic and garlic supplements have been studied in humans; however, systematic reviews and meta-analyses of randomized clinical trials (RCTs) of its effects on the cardiovascular (CV) system have reached differing results, likely due to confounding factors and/or methodological issues.

The authors performed an umbrella review of meta-analyses published between 1966 and June 2015 and found in a search of the electronic database PubMed (n=37), regardless of language, synthesizing data from observational studies and RCTs. Although dates from 1966 to June 2015 were searched, the earliest meta-analysis found was published in 1993. A hand search of references and relevant clinical guidelines identified three other records. Twelve were excluded because they were abstracts only, concerned animals, or were irrelevant, and 12 more were not meta-analyses, leaving 16 for inclusion. Of these, nine concerned effects of garlic on lipid parameters; eight, effects on BP (one meta-analysis addressed both). Systematic reviews analyzed included meta-analyses of RCTs and crossover and observational studies; reported garlic intake and highest vs. lowest intake level; had study populations of adults who were >18 years, healthy, patients with DT2, obese, overweight, hypertensive, had impaired glucose metabolism, or had CVD; and reported outcome measures including blood lipids, glycemic control, BP, inflammation markers, and CV events and/or mortality. Review quality was rated using a version of the Overview Quality Assessment Questionnaire (OQAQ), including a bias tool. Quality was moderate to good across all studies. The number of studies included in each meta-analysis

ranged from two to 35; the number of subjects ranged from 87 to 2298. Duration of interventions was seven to 84 days. Reviews were in some cases based on overlapping sets of studies. Given the heterogeneity of nutritional intervention studies, it is "not surprising" that the literature concerns many types of garlic products and study populations. The authors extracted data where possible.

Eight of nine meta-analyses of the effects of garlic on blood lipids reported significantly reduced total cholesterol (TC) levels, while one reported no significant effect. The effect of garlic on triglycerides lasted for three months after intervention in one analysis. The effect of garlic on high-density lipoprotein cholesterol (HDL-C) was modest, and in six of seven meta-analyses considering that value did not reach significance. A meta-analysis using data from 2298 subjects in 30 trials found small increases in HDL-C and, through subgroup analysis, that garlic oil gave the most benefit. In three of six meta-analyses examining low-density lipoprotein cholesterol (LDL-C) levels, levels significantly dropped after garlic use; three reported no effect on LDL-C. Three of five meta-analyses reported a significant decrease in triglycerides. Subgroup analyses in some meta-analyses found that garlic's effects on TC were significantly greater in patients with hypercholesterolemia.

Seven of eight meta-analyses found a "substantial decrease" in systolic BP (SBP) after garlic administration, and six of eight reported a significant decrease in diastolic BP. The studies included in these meta-analyses included subjects with substantial differences in baseline BP levels. Two meta-analyses found more pronounced reductions in SBP in subjects with higher baseline SBP, meaning that the use of normotensive individuals in studies obscures the potential benefit.

Only a few RCTs to date have studied garlic's effects on glycemic control parameters, and only one meta-analysis has synthesized data from them. That meta-analysis reported a significant average decrease (18 mg/dL) in fasting blood glucose in 27 trials, including four RCTs that enrolled patients with DT2 or hypercholesterolemia.

While garlic's adverse effects (AEs) are usually of a subjective nature (bad breath, body odor, bad taste), mild gastrointestinal AEs have been reported. Serious AEs such as delayed hemostasis or allergy (skin rashes, etc.) have been reported only rarely.

An issue that may affect the relevance of these results is the variety of garlic preparations and dosages used in included studies. Garlic powder was most used, at 600-2400 mg/day, stated to equate to 3.6-13.6 mg/d allicin. Fresh garlic cloves were used in others. In fresh garlic, levels of allicin derivatives vary with the preparation method, since they are released only through mechanical destruction of garlic cells, an enzymatic process whose rate can be affected by ambient temperature and/or pH. No meta-analysis provided detailed information about the variation among studies in garlic chemical content due to preparation differences. The authors suggest that it would be desirable if future RCTs more consistently used similar types and dosages of garlic products (however, they do not recommend products or dosages to be preferred).

—Mariann Garner-Wizard

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