Q/ Does evidence support the use of supplements to aid in BP control?

EVIDENCE-BASED ANSWER

A/ Yes. A number of well-tolerated natural therapies have been shown to reduce systolic and diastolic blood pressure (BP). (See TABLE1-8 for summary.) However, the studies don’t provide direct evidence of whether the decrease in BP is linked to patient-oriented outcomes. Nor do they allow definitive conclusions concerning the lasting nature of the reductions, because most studies were fewer than 6 months in duration (strength of recommendation: C, disease-oriented evidence).

Evidence summary

 Cocoa. A 2017 Cochrane review evaluated data from more than 1800 patients (401 in hypertension studies) to determine the effect of cocoa on BP.1 Compared with placebo (in flavanol-free or low-flavanol controls), cocoa lowered systolic BP by 1.8 mm Hg (confidence interval [CI], −3.1 to −0.4) and diastolic BP by 1.8 mm Hg (CI, −2.6 to −0.9). Further analysis of patients with hypertension (only) showed a reduction in systolic BP of 4 mm Hg (CI, −6.7 to −1.3).

 Omega-3 fatty acids. Similarly, a 2014 meta-analysis investigating omega-3 fatty acids (eicosapentaenoic acid [EPA] + docosahexaenoic acid [DHA]) included data from 4489 patients (956 with hypertension) and showed reductions in systolic BP of 1.5 mm Hg (CI, −2.3 to −0.8) and diastolic BP of 1 mm Hg (CI, −1.5 to −0.4), compared with placebo.2 Again, subgroup analysis of patients with hypertension (only) at baseline revealed a greater decrease in systolic and diastolic BP: 4.5 mm Hg (CI, −6.1 to −2.8) and 3.1 mm Hg (CI, −4.4 to −1.8), respectively.

 Garlic and potassium chloride. Separate meta-analyses that included only patients with hypertension found that both garlic and potassium significantly lowered BP.3,4 A 2015 meta-analysis comparing a variety of garlic preparations with placebo in patients with hypertension showed decreases in systolic BP of 9.1 mm Hg (CI, −12.7 to −5.4) and in diastolic BP of 3.8 mm Hg (CI, −6.7 to −1).3 Meanwhile, a meta-analysis in 2017 comparing different doses of potassium chloride with placebo demonstrated reductions in systolic BP of 4.3 mm Hg (CI, −6 to −2.5) and diastolic BP of 2.5 mm Hg (CI, −4.1 to −1).4

 L-arginine. Another meta-analysis of randomized controlled trials reported evidence that oral L-arginine, compared with placebo, significantly reduced systolic BP by 5.4 mm Hg (CI, −8.5 to −2.3) and diastolic BP by 2.7 mm Hg (CI, −3.8 to −1.5).5 Close to one-third of patients had hypertension at baseline.

 Beetroot juice. A double-blind, placebo-controlled study showed that consumption of beetroot juice (with nitrate) once daily reduced BP in 3 different settings (clinic, 24-hour ambulatory, and home readings) when compared with placebo (nitrate-free beetroot juice).6 Study participants were mostly British women, overweight, without significant cardiovascular or renal disease, and with uncontrolled ambulatory BP (> 135/85 mm Hg).

 Flax seed. A prospective, double-blind trial of patients with peripheral artery disease compared the antihypertensive effects...
<table>
<thead>
<tr>
<th>Therapy (study type)</th>
<th>Subjects</th>
<th>Dose</th>
<th>Duration (wk)</th>
<th>Adverse effects</th>
<th>Effect on BP, reduction in mm Hg</th>
<th>Comments</th>
</tr>
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</table>
| Beetroot/nitrate<sup>6</sup> (RCT) | 68 (all with HTN; half drug naïve and half medication treated) | Beetroot juice 250 mL/d (~ 6.4 mmol nitrate) | 4 | Beeturia and fecal discoloration (mild) | Mean: SBP = 7.7 (CI, -11.8 to -3.6; \( P < .001 \))
DBP = 2.4 (CI, -4.9 to 0.0; \( P = .050 \))
24-hr BP:
SBP = 7.7 (CI, -11.2 to -4.1; \( P < .001 \))
DBP = 5.2 (CI, -7.7 to -2.7; \( P < 0.001 \))
Home BP:
SBP = 8.1 (CI, -12.4 to -3.8; \( P < .001 \))
DBP = 3.8 (CI, -6.9 to -0.7; \( P < .01 \)) | No nitrate-associated tachyphylaxis was noted |
| Cocoa<sup>1</sup> (SR/MA) | 1804 (401 with HTN) | 1.4-105 g/d of cocoa products | 2-18 (mean, 9) | Mild GI symptoms including nausea | SBP = 1.8 (CI, -3.1 to -0.4)
DBP = 1.8 (CI, -2.6 to -0.9) | Moderate-quality evidence; moderate-high heterogeneity; mild reporting bias |
| Flax seed<sup>7</sup> (prospective RCT) | 110 (all with HTN) | 30 g/d | 24 | Similar to placebo | SBP = 10 (\( P = .04 \))
DBP = 7 (\( P = .004 \)) | All patients had PAD; BP reductions were more pronounced in patients with HTN |
| Garlic<sup>3</sup> (SR/MA, 9 RCTs) | 482 (all with HTN) | 240-2400 mg/d (aged extract, garlic oil, garlic powder, egg yolk–enriched garlic powder) | 8-26 (mean, 13.5) | Mild GI symptoms such as burping, flatulence, and reflux | SBP = 9.1 (CI, -12.7 to -5.4; \( P = .0006 \))
DBP = 3.8 (CI, -6.7 to -1; \( P = .00001 \)) | Quality of included trials was moderate; moderate-high heterogeneity; insufficient data to determine publication bias |
| L-arginine<sup>5</sup> (SR/MA, 11 RCTs) | 387 (1/3 with baseline HTN) | 4-24 g/d (mean, 9 g/d) | 2-24 (mean, 4) | Diarrhea | SBP = 5.4 (CI, -8.5 to -2.3; \( P = .001 \))
DBP = 2.7 (CI, -3.8 to -1.5; \( P < .001 \)) | All studies were double-blind; BP primary outcome in 5 studies; moderate heterogeneity; greater BP reduction in patients with higher baseline BP |
| Olive leaf<sup>8</sup> (RCT) | 148 (all with HTN) | Olive leaf extract 500 mg bid; captopril 12.5-25 mg | 8 | Cough, vertigo, myalgias, and headache (mild and similar between groups) | Olive leaf extract:
SBP = 11.5 ± 8.6
DBP = 4.8 ± 5.5
Captopril:
SBP = 13.7 ± 7.6
DBP = 6.4 ± 5.2 (Difference between treatments \( P > .05 \)) | Study excluded patients with signs of target organ damage (eg, heart, kidneys, liver) |

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of flax seed with placebo in patients with and without hypertension and found marked decreases in systolic and diastolic BP.7 Study participants were all older than 40 years without other major cardiac or renal disease, and the majority of enrolled patients with hypertension were concurrently taking medications to treat hypertension during the study.

**Olive leaf extract.** A double-blind, parallel, and active-control clinical trial in Indonesia compared the BP-lowering effect of olive leaf extract (*Olea europaea*) to captopril as monotherapies in patients with stage 1 hypertension.8 After a 4-week period of dietary intervention, individuals who were still hypertensive (range, 140/90 to 159/99 mm Hg) were treated with either olive leaf extract or captopril. After 8 weeks of treatment, both groups saw comparable reductions in BP.

**Editor’s takeaway**
Many studies have demonstrated BP benefits from a variety of natural supplements. Although the studies’ durations are short, the effects sometimes modest, and the outcomes disease-oriented rather than patient-oriented, the findings can provide a useful complement to our efforts to manage this most common chronic disease.

**References**
2. Miller PE, Van Elswyk M, Alexander DD. Long-chain omega-3 fatty acids eicosapentaenoic acid + docosahexaenoic acid; GI, gastrointestinal; HTN, hypertension; KCl, potassium chloride; NA, not available; NR, not reported; PAD, peripheral artery disease; RCT, randomized controlled trial; SBP, systolic blood pressure; SR/MA, systematic review and meta-analysis.

**TABLE**
How well do these supplements aid in BP control? (cont’d)

<table>
<thead>
<tr>
<th>Therapy (study type)</th>
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<tbody>
<tr>
<td>Omega-3 fatty acids (EPA+DHA)2 (SR/MA, 70 RCTs)</td>
<td>4489 (956 with HTN)</td>
<td>EPA+DHA dose: 0.1-15 g/d (mean, 3.8 g/d)</td>
<td>4-52 (mean, 10)</td>
<td>NR</td>
<td>Overall: SBP = 1.5 (CI, –2.3 to –0.8); DBP = 1 (CI, –1.5 to –0.4)</td>
<td>All trials were double-blind; low heterogeneity; mild publication bias</td>
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<td>Potassium4 (SR/MA, 23 RCTs)</td>
<td>1213 (all with HTN)</td>
<td>6-200 mEq of KCl daily</td>
<td>4-52</td>
<td>Abdominal pain, nausea, vomiting, diarrhea, gas. (mild, similar to placebo)</td>
<td>SBP = 4.3 (CI, –6.0 to –2.5; ( P &lt; .00001 )); DBP = 2.5 (CI, –4.1 to –1.0; ( P &lt; .001 ))</td>
<td>Mild-moderate heterogeneity; low bias; showed dose-response relationship</td>
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BP, blood pressure; CI, 95% confidence interval; DBP, diastolic blood pressure; EPA+DHA, eicosapentaenoic acid + docosahexaenoic acid; GI, gastrointestinal; HTN, hypertension; KCl, potassium chloride; NA, not available; NR, not reported; PAD, peripheral artery disease; RCT, randomized controlled trial; SBP, systolic blood pressure; SR/MA, systematic review and meta-analysis.