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Garlic, Chocolate, or Tomatoes for (Pre-) Hypertension?

K Ried

Abstract: Aged garlic extract, dark chocolate, or lycopene-rich tomato products have been linked with blood pressure-lowering properties in hypertensive people. There is consistent evidence for garlic supplements, in particular in the form of Kyolic® aged garlic extract, to be effective in lowering blood pressure comparable to first-line standard antihypertensive medication.

Dark chocolate appears to be beneficial for blood pressure reduction as well, albeit to a lesser extent than Kyolic®. Lycopene in tomato extract has a protective effect on serum cholesterol similar to low-dose statins, and may also be beneficial for lowering blood pressure in hypertensive people.

Key words: uncontrolled hypertension, non-pharmacological treatment, Kyolic® aged garlic extract, cocoa, chocolate, lycopene, tomato, cholesterol, meta-analysis

Kurzfassung: Knoblauch, Schokolade oder Tomaten für (Vorstadien des) Bluthochdruck(s)? Gealterter Knoblauchextrakt, dunkle Schokolade oder lycopinreiche Tomatenprodukte sind mit blutdrucksenkenden Eigenschaften bei Hypertonikern in Verbindung gebracht worden. Es gibt beständige Evidenz, dass Knoblauch-Nahrungsergänzungen, vor allem in der Form von Kyolic® gealtertem Knoblauchextrakt, in einem vergleichbaren Ausmaß effektiv den

Blutdruck senken wie eine antihypertensive First-line-Medikation.

Dunkle Schokolade scheint ebenso förderlich bei der Blutdrucksenkung zu sein, wenn auch in einem geringeren Ausmaß als Kyolic®. Lycopin in Tomatenextrakt hat einen protektiven Effekt auf das Serum-Cholesterin, der vergleichbar ist mit niedrig dosierten Statinen, und mag auch förderlich sein, um den Blutdruck bei Hypertonikern zu senken. **J Hypertonie 2011; 15 (3): 7–10.**

Schlüsselwörter: unkontrollierte Hypertonie, nicht-pharmakologische Behandlung, Kyolic® gealterter Knoblauchextrakt, Kakao, Schokolade, Lycopin, Tomate, Cholesterin, Metaanalyse

■ Background

Hypertension is a critically important risk factor for cardiovascular morbidity and mortality. Lifetime risk (> 50 years) of suffering a cardiovascular event, such as myocardial infarction or stroke, is 3–7 times higher among patients with high blood pressure (systolic [SBP]/diastolic [DBP] > 140/90 mmHg) compared to patients with a blood pressure of < 120/80 mmHg [1, 2]. The risk for mortality from both ischemic heart disease and stroke is estimated to double for every 20 mmHg rise in SBP and 10 mmHg in DBP [3]. The association between blood pressure and cardiovascular risk is continuous, and even small reductions in blood pressure substantially reduce cardiovascular risk [4].

Current standard therapy of hypertension involves pharmacological treatment, including angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor antagonists (A2RA), calcium channel blockers (CCB), diuretics (D), and beta-blockers (BB) [5]. Approximately 40 % of hypertensive patients achieve the target blood pressure of < 140/90 mmHg with monotherapy, about 40 % require combination therapy with 2 agents, and 20 % need to take ≥ 3 antihypertensive medications to achieve blood pressure control [6].

However, adverse reactions from antihypertensive medication may occur in a significant number of patients and are more likely when multiple drugs are prescribed [7, 8]. Adverse reactions including fatigue, dizziness, cough, headache, myalgia, angioedema, renal impairment, gastrointestinal upsets as well as hyperglycaemia, and electrolyte disturbances

can be serious and may require hospitalisation [7, 8]. Complexity of treatment, frequency and severity of adverse effects influence long-term persistence to treatment, and control of blood pressure may also be hampered by therapeutic inertia [5, 8, 9].

Non-pharmacological agents, such as garlic supplements, cocoa, and tomato products have been linked with blood pressure-lowering properties and high tolerability and may provide an alternative or complementary treatment option for hypertension. This article summarises current evidence and compares effectiveness, acceptability, and practicability of 3 non-pharmacological treatment options for hypertension.

■ Methods

Our team has conducted meta-analyses as well as clinical trial research on the effect of garlic supplements, cocoa, or lycopene-rich tomato products on blood pressure [10–14]. Subgroup meta-analyses provide evidence for their effectiveness dependent on hypertension status. In addition, we summarise acceptability and practicability of long-term treatment and provide a systematic review of diverse garlic supplements, cocoa, and lycopene-rich products on the market.

■ Results and Discussion

Garlic

Meta-analyses by our research team and others including 14 primary studies of approximately 700 participants found garlic supplements to be superior to placebo in lowering blood pressure in hypertensive untreated patients (mean change in SBP ± SE [standard error]: -8.4 ± 2.8 mmHg; mean change DBP: -7.3 ± 1.5 mmHg; $p < 0.0001$) [10, 15], but not in people with prehypertension or normal blood pressure. The reduction in blood pressure in hypertensive patients is comparable to the blood pressure-lowering effects of common prescription medications and has implications at a population level, where a reduction of 4–5 mmHg in SBP and 2–3 mmHg

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in DBP has been estimated to reduce the risk of cardiovascular morbidity and mortality by 8–20 % [2, 4].

In addition, our team conducted a double-blind parallel randomised placebo-controlled trial involving 50 general-practice patients with treated but uncontrolled hypertension testing the effect of aged garlic extract on blood pressure [11].

Patients enrolled in the trial received the trial medication in addition to their standard antihypertensive medication. The active group received aged garlic extract (Kyolic® High Potency Everyday Formula 112, Wakunaga [16]), 4 capsules containing 960 mg aged garlic extract and 2.4 mg S-allylcysteine (SAC) daily for 12 weeks, and the control group received matched placebo capsules.

Our trial suggests Kyolic® aged garlic extract taken daily to be superior to placebo in reducing blood pressure in treated uncontrolled hypertensive patients [-10.2 ± 4.3 mmHg SBP; $p = 0.03$], but not in prehypertensive patients. This reduction in blood pressure is clinically significant and similar to first-line medication. Additionally, we found high acceptability and tolerability of the trial capsules (92 %) [11].

Garlic taste or odour was avoided if capsules were taken with food. A small number of patients (6 %) may experience mild gastrointestinal complaints, such as flatulence, bloating, or nausea with therapeutic doses of garlic as reported in our study and by others [11, 17]. Lower tolerance of sulphur-containing foods such as garlic, onion, and leek may be reversed by supplementation with molybdenum and/or vitamin B₁₂, often deficient in these patients [18, 19].

Garlic extract has been associated with blood pressure-lowering properties, and the mechanism of action is biologically plausible. Organic sulphur compounds in garlic block angiotensin II production and mediate intracellular nitric oxide (NO) and hydrogen sulphide (H₂S) production, which in turn promote vasodilation and thus reduction in blood pressure, as shown in human and animal studies [20–24].

The right choice of garlic supplement is important to achieve blood pressure-reducing effects. Not all types of garlic have blood pressure-lowering properties. Cooking of fresh garlic cloves destroys the active components, and raw garlic can be toxic if taken in high therapeutic doses [25]. Garlic oils and garlic macerates do not contain the components influencing blood pressure. However, garlic supplements containing the water-soluble fraction of garlic, such as garlic powder and aged garlic extract, are highly tolerable with biologically active blood pressure-reducing properties.

Aged garlic extract, available on the market as Kyolic®, is the supplement of choice and superior to garlic powder. The active ingredient in Kyolic® is S-allylcysteine (SAC), which is stable and dosage can be controlled. The 20-month long ageing and extraction process of Kyolic® eliminates odour, toxicity, and haemorrhage-causing, oil-soluble, sulphur compounds. The safety profile of Kyolic® is high, and no adverse effects have been reported if taken with other anti-thrombotic medication [26, 27].

Chocolate

Dark chocolate and flavanol-rich cocoa products have attracted interest as an alternative treatment option for hypertension. Our meta-analysis of 15 trial arms of approximately 600 participants suggests cocoa-products to have a blood pressure lowering effect in systolic hypertension and diastolic prehypertension (mean SBP change \pm SE: -5.0 ± 3.0 mmHg; $p = 0.0009$; mean DBP change \pm SE: -2.7 ± 2.2 mmHg; $p = 0.01$) [13]. The relatively modest but significant blood pressure-lowering effect of cocoa in the hypertensive subgroup is clinically relevant, and is comparable to other lifestyle modifications, such as moderate physical activity (30 minutes/day), which may reduce SBP by 4–9 mmHg [5].

The blood pressure-lowering properties of cocoa-containing products have been associated with its flavanol content which influences formation of endothelial nitric oxide, promotes vasodilation, and consequently lowers blood pressure [6–8]. To date, trials have used dark chocolate with 50–70 % cocoa, or especially formulated cocoa drinks or capsules and dosages ranged between 6–100 g daily, which is equivalent to 30–1000 mg of flavanol.

However, practicability of chocolate as a long-term treatment option is debateable. In a trial by our team using 50 grams of 70 % cocoa-containing chocolate daily, 30 % of participants found this an unacceptable long-term treatment option [12, 28]. In addition, chocolate is high in sugar (~ 30–50 % by weight) and fat (~ 20–50 % by weight), and thus high in calories (480–540 kcal). Chronic unbalanced intake may increase energy intake and potentially body weight, which counteracts blood pressure-lowering effects. While participants in our study did not gain weight over a 3-month period with 50 g of dark chocolate daily intake [12], participants in another study consuming 25 g of chocolate daily for 3 months gained 0.8 kg on average during the study period [29].

Tomato

Lycopene, a carotenoid without provitamin-A activity, is the pigment responsible for the distinctive red colour in tomatoes and watermelon, and is also found in pink grapefruit, papaya, guava, and rosehip [30–32]. Generally, riper and deeper red fruit and vegetables contain more lycopene, and cooking and processing further increase lycopene content and bioavailability [33–35]. High lycopene consumption has been associated with a decreased risk of cardiovascular disease, including atherosclerosis, myocardial infarction, and stroke [36–39]. Etiology of cardiovascular disease is related to oxidative stress, inflammatory processes, endothelial dysfunction, and subsequent vascular remodelling. Lycopene has been shown to lower oxidative stress by reducing the oxidation of LDL cholesterol and subsequent inflammation and atherosclerotic plaque formation [40, 41].

Lycopene-rich tomato extract (Lyc-O-Mato® by LycoRed, one capsule contains 15 mg of lycopene [42]) has shown promise to reduce blood pressure in hypertensive patients (-9.4 ± 1.7 mmHg SBP; $p < 0.0001$), but not prehypertensive patients [14, 43, 44]. More research is currently being conducted to ascertain blood pressure-lowering mechanism and effect [45]. Tolerability and safety of tomato extract capsules

in dosages of 15–30 mg lycopene daily is extremely high, with no adverse effects reported in published trials [12, 43, 44].

Evidence of a protective effect of lycopene on blood lipids is stronger. A meta-analysis by our team including 15 trials of approximately 700 participants suggests lycopene to be effective in reducing LDL cholesterol and total serum cholesterol if taken in doses > 25 mg daily (mean LDL cholesterol change \pm SE: -10.35 ± 5.64 mg/dl [0.27 ± 0.15 mmol/l; $p = 0.0003$]) [14].

Twenty-five milligrams of lycopene are equivalent to 500 ml of tomato juice, 50 g of tomato paste, or 2 capsules of Lyc-O-Mato® tomato extract. Larger dosages of lycopene up to 200 mg daily long-term appear to cause minimal side effects. A rare but reversible condition of orange discoloration of the

palms (lycopenemia) has been described in one individual who consumed 2 litres of tomato juice daily over several years [46].

The LDL cholesterol-reducing effect of about 10 % achieved with daily dosages of ≥ 25 mg of lycopene is clinically significant and comparable to the effect of low-dose statins. While statins are highly effective cholesterol-lowering medications, side effects including muscle pain, muscle weakness, and neuropathy are experienced by some patients [47–49].

Lycopene reduces LDL cholesterol by suppression of cholesterol synthesis, increase of LDL degradation, and inhibition of HMG-CoA-reductase, without the side effects of statin drugs [50]. Our research suggests that lycopene may be considered as alternative to low-dose statins in patients with slightly elevated cholesterol levels.

■ Conclusions and Relevance to Practice

There is strong evidence to suggest garlic supplements to be an effective alternative or complementary treatment for hypertension. The blood pressure-reducing effect is comparable to first-line standard antihypertensive medication. Aged garlic extract, also known as Kyolic®, is the supplement of choice with a high safety profile if taken as a sole treatment or in addition to standard medication for hypertension.

There is evidence to support a beneficial effect of cocoa products including dark chocolate on hypertension. The blood pressure-reducing effect achieved with regular consumption of cocoa products is lower compared with aged garlic extract but comparable to the effect achieved with lifestyle modifications such as regular exercise. However, practicability of chocolate as a treatment option is debatable, due to associated calorie intake.

Lycopene in tomato extract has cholesterol-lowering properties similar to low-dose statins and may be considered as alternative treatment for patients with slightly elevated cholesterol levels. Current evidence is promising for a beneficial effect of lycopene for hypertension, warranting further research.

Current evidence is inconclusive regarding a preventive role of garlic extract, chocolate or tomato extract to halt the progression of prehypertension to hypertension. Larger and longer-term studies are needed to elucidate whether these functional foods could be used as preventive remedies.

■ Conflict of Interest

None.

■ Relevanz für die Praxis

Die Evidenz ist stark, dass Knoblauch-Nahrungsergänzungen eine effektive Alternative oder komplementäre Behandlung für die Hypertonie sind. Der blutdrucksenkende Effekt ist vergleichbar mit einer antihypertensiven Standard-First-line-Therapie. Gealterter Knoblauchextrakt, auch bekannt als Kyolic®, ist die Nahrungsergänzung der Wahl mit einem hohen Sicherheitsprofil, wenn es als alleiniges Mittel oder zusätzlich zu einer Standardmedikation für Hypertonie eingenommen wird.

Es gibt Evidenz, die den förderlichen Effekt von Kakaoprodukten inklusive dunkler Schokolade auf die Hypertonie unterstützt. Der durch regelmäßige Einnahme von Kakaoprodukten erreichte blutdrucksenkende Effekt ist geringer im Vergleich zu gealtertem Knoblauchextrakt, aber vergleichbar zu dem Effekt durch Lebensstilmodifikationen, wie z. B. regelmäßiges Training. Die Praktikabilität von Schokolade als Behandlungsoption ist jedoch infrage zu stellen aufgrund der damit verbundenen Kalorienzahl.

Lycopin in Tomatenextrakt hat cholesterinsenkende Eigenschaften, die mit jenen niedrig dosierter Statine vergleichbar sind, und kann als alternative Behandlung für Patienten mit geringfügig erhöhten Cholesterinwerten angesehen werden. Die gegenwärtige Evidenz ist vielversprechend für einen förderlichen Effekt von Lycopin auf die Hypertonie, erfordert jedoch noch weitere Erforschung.

Die gegenwärtige Evidenz ist nicht schlüssig, was die präventive Rolle von Knoblauchextrakt, Schokolade oder Tomatenextrakt beim Fortschreiten der Prähypertonie zur Hypertonie betrifft. Größere und über einen längeren Zeitraum angelegte Studien sind notwendig, um festzustellen, ob diese „functional foods“ als präventive Mittel eingesetzt werden können.

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