Effect of garlic powder on C-reactive protein and plasma lipids in overweight and smoking subjects

Martijn BA van Doorn, Sonia M Espirito Santo, Piet Meijer, Ingrid M Kamerling, Rik C Schoemaker, Verena Dirsch, Angelika Vollmar, Thomas Haffner, Rolf Gebhardt, Adam F Cohen, Hans M Princen, and Jacobus Burggraaf

ABSTRACT
Background: Epidemiologic studies suggest that garlic may have beneficial effects on risk factors associated with cardiovascular disease (CVD). However, these findings are not unambiguously supported by randomized placebo-controlled clinical trials.

Objective: We sought to investigate the effects of a chemically well-characterized garlic preparation on biomarkers for inflammation, endothelial function, and lipid metabolism in subjects with risk factors for CVD.

Design: This was a double-blind, randomized, placebo-controlled trial in 90 overweight [body mass index (in kg/m²) > 24.5] subjects aged 40–75 y who smoked >10 cigarettes/d. The subjects were randomly assigned to 3 parallel treatment groups: garlic powder (2.1 g/d), atorvastatin (40 mg/d), or placebo. Duplicate measurements were performed at baseline and after 1 and 3 mo of treatment. Treatments were compared with analysis of covariance with baseline as the covariate, and differences between the treatments were reported as mean percentage difference and corresponding 97.5% CI.

Results: None of the variables showed significant differences between the garlic-treated and the placebo groups. In contrast, compared with the placebo group, atorvastatin treatment resulted in significantly lower plasma concentrations of C-reactive protein (20.2%; 1.7%, 35.3%), total cholesterol (37.2%; 33.1%, 41.1%), LDL cholesterol (52.7%; 47.9%, 57.1%), triacylglycerols (31.9%; 20.8%, 41.5%), and tumor necrosis factor α (TNF-α; 41.9%; 19.0%, 58.3%) and increased the ratio of ex vivo whole blood lipopolysaccharide-stimulated to nonstimulated TNF-α concentrations (109.7%; 37.9%, 218.9%).

Conclusion: We conclude that a chemically well-characterized garlic preparation has no significant effect on inflammatory biomarkers, endothelial function, or lipid profile in normolipidemic subjects with risk factors for CVD.

KEY WORDS Garlic, C-reactive protein, CRP, lipids, endothelial function, humans

INTRODUCTION
Beneficial effects of garlic on human health have been claimed for decades. One claim entails the beneficial effects of garlic on risk factors associated with atherosclerosis and, consequently, on the occurrence of cardiovascular events (1, 2). To support this, several studies found a lowering of plasma lipid concentrations, systolic blood pressure, arterial stiffness, and enhanced fibrinolytic activity to be associated with garlic use (3–8). Through these actions, garlic is believed to prevent progressive atherosclerotic changes and consequently to reduce the incidence of cardiovascular events. However, other studies do not support these observations and reported no significant effects on these variables (9–13). These conflicting findings may be ascribed to the use of different study designs (eg, lack of placebo group), different patient inclusion criteria, and different garlic-derived material (ie, raw, powder, or oil), all of which vary in production conditions and chemical composition (14).

However, another explanation may be that garlic influences other than the classical risk factors for atherosclerosis (15). Evidence is growing to indicate that inflammation plays an important role in the pathophysiology of atherosclerosis. It has been shown that C-reactive protein (CRP) is one of the strongest predictors for the risk of atherosclerosis and cardiovascular events in subjects with and without cardiovascular disease (CVD) (16–18). To our knowledge, no studies have reported the effects of garlic on CRP or other markers of inflammation in humans. In vitro studies show that high concentrations of garlic decrease cytokine production in endothelial cells, suggesting antiinflammatory properties (19–21). Hence, investigating the effects of garlic on markers of inflammation associated with CVD may be important and provide an explanation for the alleged benefits of garlic on human health.

To further investigate the effects of garlic on various human health variables, the collaborative European Union program Garlic and Health was started. This program aimed to identify garlic species containing the highest content of the sulfur-containing compounds believed responsible for health benefits, to perform preclinical experiments with this garlic preparation to define garlic’s role on pharmacologic targets, and to investigate
the effects of a pharmaceutical garlic preparation in a clinical trial of which the results are described in this article.

Therefore, we investigated the effects of a chemically well-characterized and production-controlled garlic powder on plasma CRP concentrations (primary endpoint) in subjects with known risk factors for CVD, during 12 wk of treatment. In addition, the effects of garlic powder on plasma lipid concentrations, plasma markers of inflammation, and markers of endothelial function were investigated. The study was carried out with the use of atorvastatin as a positive control because atorvastatin was shown to decrease CRP and cholesterol concentrations in normolipidemic subjects (22, 23).

SUBJECTS AND METHODS

Subjects

The study was carried out by using a double-blind, randomized, placebo-controlled design with 3 parallel groups. The study protocol was approved by the Committee on Medical Ethics of Leiden University Medical Center (LUMC) and conducted in the Netherlands. Subjects were recruited by advertisements in local newspapers. The participants were of either sex in general good health with known risk factors for atherosclerosis [ie, age 40–75 y, smoking >10 cigarettes/d, and body mass index (in kg/m²) > 24.5]. Subjects were excluded if they used chronic (ie, hormone replacement therapy or antihypertensives) or any other medication (ie, aspirin, nonsteroidal antiinflammatory drugs, or lipid-lowering drugs) that interferes with the measures of the study. Eligibility was assessed with a general health questionnaire and measurement of body weight, height, blood pressure, and routine laboratory variables, including a urine pregnancy test for the female subjects. A total of 150 subjects were informed about the study; 142 signed the informed consent. Ninety subjects were eligible and entered the study.

Study design

Eligible subjects started with a 2-wk placebo run-in period after which blood samples for determination of liver enzymes, creatine phosphokinase (CPK), hemoglobin, viral serology (hepatitis B and C, HIV), and a urine sample for pregnancy testing (for the women) were collected. If all variables were still within the inclusion range, subjects were randomly assigned to 1 of the 3 treatment arms. The subjects received either the garlic preparation (daily dose of 2.1 g; three 300-mg garlic tablets in the morning and four 300-mg garlic tablets in the evening plus 1 atorvastatin-matching placebo tablet) or atorvastatin (daily dose of 40 mg; 3 garlic-matching placebo tablets in the morning and 4 garlic-matching placebo tablets in the evening plus a 40-mg atorvastatin tablet) or placebo (3 garlic-matching placebo tablets in the morning and 4 garlic-matching placebo tablets in the evening plus 1 atorvastatin-matching placebo tablet in the evening). The total treatment period was 12 wk with follow-up visits scheduled after 4, 5, 11, and 12 wk. On these visits the subjects reported to the research unit after an overnight fast where their medical history was taken; adverse events were recorded. Also, the study medication was counted, vital signs were measured, and blood samples were taken.

Treatments

The garlic powder (Printanor) was produced under high sulfur-fertilization levels during the cultivation procedures as a part of the European Union research program Garlic and Health carried out by a consortium of 15 independent research groups from 6 countries. This garlic powder was produced and supplied by one of the participants (INRA, Dijon, France) and analyzed by standard HPLC procedure for the content of garlic sulfur-containing compounds (ie, allicin liberation capacity) (14). The allicin liberation capacity was 4.5 μg allicin/mg garlic powder. This means that the subjects with a daily intake of 2.1 g garlic powder/d had the capacity to liberate 9.4 mg allicin/d. Subsequently, 300-mg tablets of this garlic powder and matching placebo tablets were produced under good manufacturing practice standards (Lichtwer Pharma AG, Berlin, Germany). The tablets were enteric coated, such that the tablets were (gastric) acid resistant for at least 2 h (24). Atorvastatin (Lipitor 40 mg) tablets were purchased by the LUMC hospital pharmacy, and matching placebo tablets were manufactured (Katwijk Pharma, Katwijk, Netherlands). All study medication was packed, labeled, and dispensed by the LUMC pharmacy.

Measurements

Tolerability assessment consisted of adverse event assessment, measurements of vital signs, 12-lead electrocardiogram recordings (Cardiofax V equipped with ECAPS12 analysis program; Nihon Kohden, Tokyo, Japan) and routine laboratory safety measurements (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, γ-glutamyl transpeptidase, lactate dehydrogenase, CPK, total bilirubin, and conjugated bilirubin) on all visits.

Blood sampling and assays

All blood samples were collected at screening, at random assignment, after 4 and 5 wk (1 mo) of treatment, and after 11 and 12 wk (3 mo) of treatment. The samples were taken after an overnight fast and at least 10 min of supine rest. Blood samples for hemoglobin concentration (at screening) were collected in tubes containing EDTA and measured by the Central Clinical Hematology Laboratory of LUMC with the use of a standard automated assay. Blood samples for aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, γ-glutamyl transpeptidase, lactate dehydrogenase, CPK, bilirubin, cholesterol, HDL cholesterol, LDL cholesterol, and triacylglycerols (at screening and during study) were collected in plain serum tubes and measured by the Central Clinical Chemistry Laboratory of LUMC with the use of standard methods. Blood samples for CRP, von Willebrand factor, and fibrinogen (STA fibrinogen methods; Roche Diagnostics, Mannheim, Germany) were collected on ice in tubes containing 0.105 M citrate and processed within 60 min and measured by using previously described methods (25, 26). Blood samples for tumor necrosis factor α (TNF-α) were collected in tubes containing EDTA, stored at 37 °C, and processed within 30 min. TNF-α was measured with the use of the Quantikine TNF-α enzyme-linked immunoabsorbent assay (R&D Systems, Abington, United Kingdom) in EDTA plasma of a whole blood lipopolysaccharide stimulation test with the use of 0 and 10 ng lipopolysaccharide/mL (final concentration) and overnight incubation at 37 °C in a 5% CO₂ incubator (27). Blood samples for markers of vessel wall activation (soluble vascular cell adhesion molecule, soluble intercellular adhesion molecule, and soluble selectin) were collected on ice in Li-Heparin tubes, processed within 60 min, and measured by commercial kits (R&D Systems).
TABLE 1
Baseline characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Placebo group</th>
<th>Garlic group</th>
<th>Atorvastatin group</th>
<th>P at baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>16</td>
<td>17</td>
<td>NA</td>
</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>12</td>
<td>13</td>
<td>0.5497</td>
</tr>
<tr>
<td>Age (y)</td>
<td>48.8 ± 6.6</td>
<td>48.5 ± 6.9</td>
<td>47.1 ± 5.6</td>
<td>0.7580</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.8 ± 3.3</td>
<td>29.1 ± 3.1</td>
<td>29.7 ± 4.3</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>124.7 ± 13.7</td>
<td>128.4 ± 13.5</td>
<td>123.0 ± 14.3</td>
<td>0.3308</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>78.8 ± 9.9</td>
<td>81.5 ± 11.5</td>
<td>72.6 ± 11.0</td>
<td>0.0080</td>
</tr>
</tbody>
</table>

1 NA, not applicable.
2 x ± SD (all such values).

Statistics

The a priori power of the study was calculated with the use of data from an earlier experiment that investigated the effects of atorvastatin on plasma CRP concentrations (26). On the basis of that data, the present study had a power of 0.72 to detect a 25% decrease in CRP or 0.80 to detect a 30% decrease in CRP (at a 2-sided α level of 0.05) in each treatment group of 30 subjects.

Data were initially analyzed by calculating change from baseline and including the values after baseline only, with the use of SAS PROC MIXED with an unstructured covariance matrix, with subject as random effect, time and treatment by time interaction as fixed effects, and with baseline and baseline by time as covariates. The treatment-by-time interaction tests for overall parallel time profiles. Subsequently, the endpoints were analyzed by mixed-model analyses of covariance (with the use of SAS PROC MIXED with an unstructured covariance matrix) with subject as a random effect; treatment, time, and treatment-by-time as fixed effects; and with baseline as covariate. Data were analyzed and log-transformed to correct for the observed log-normal distribution of the data (which is common for concentration measurements). The analysis results were back-transformed and presented as geometric mean and percentage of difference and the corresponding 97.5% CI for the treatment contrasts. To correct for multiple comparisons of the 2 prespecified contrasts, P values < 0.025 were considered statistically significant, and contrasts are reported with 97.5% CIs. In addition, baseline variables were compared by using analysis of variance. All calculations were performed with the use of SAS for WINDOWS version 9.1.2 (SAS Institute Inc, Cary, NC).

RESULTS

Ten subjects (3 subjects in the atorvastatin group, 5 subjects in the garlic group, and 2 subjects in the placebo group) did not complete the study because of personal reasons (n = 3) or adverse events (n = 7). Two of these adverse events (abdominal discomfort and severe garlic odor) occurred in subjects randomly assigned to receive garlic, whereas the remaining 5 events were considered unrelated. Five of these subjects did contribute data to the analysis because they provided data at the 1-mo assessment. Two subjects (in the atorvastatin group) were replaced with newly recruited volunteers. In addition, 3 subjects were excluded from the statistical analysis before unblinding (all 3 in the placebo group) because of intermittent inflammatory conditions, which were expected to interfere with the assessment of CRP status.

Therefore, the final study population consisted of 84 subjects; 30 subjects in the atorvastatin group, 28 subjects in the garlic group, and 26 subjects in the placebo group. Characteristics of the study population are listed in Table 1. No significant differences were observed in the baseline characteristics among the 3 groups except for diastolic blood pressure, which was slightly lower in the atorvastatin group. This difference in diastolic blood pressure was considered not physiologically important.

Adverse events

The adverse events reported in the course of the present study were mild or moderate and considered unrelated to study drug administration except for the severe garlic odor. Vital signs, electrocardiogram, and routine laboratory variables were virtually unchanged apart from a mild rise in liver enzyme concentrations noted in the atorvastatin group.

Compliance

The compliance data showed only minor differences among subjects in tablet counts of returned study medication on each visit. The average daily intake of garlic was 7.1 ± 0.1 tablets (range: 6.9–7.2 tablets), and the average daily intake of atorvastatin was 1.0 ± 0.1 tablets (range: 0.9–1.2 tablets).

Inflammation markers

During 12 wk of garlic treatment, the mean CRP concentration increased nonsignificantly by 17.8% (97.5% CI: −5.0%, 46.0%) compared with placebo treatment; whereas atorvastatin treatment resulted in a 20.2% (97.5% CI: 1.7%, 35.3%) decrease in mean CRP concentration compared with placebo treatment (Table 2). After garlic treatment, plasma (nonstimulated) TNF-α concentrations and the ratio between lipopolysaccharide-stimulated and nonstimulated TNF-α concentrations remained virtually unchanged. In contrast, after atorvastatin treatment, a significantly lower mean plasma TNF-α concentration and higher ratio of the lipopolysaccharide-stimulated concentration to nonstimulated mean TNF-α concentration was observed (Table 2). Plasma fibrinogen concentrations were unaffected in both the garlic and the atorvastatin treatment groups (Table 2).

Endothelial function markers

Neither garlic nor atorvastatin treatments affected the mean plasma concentrations of von Willebrand factor, soluble vascular cell adhesion molecule, soluble intercellular adhesion molecule, and soluble selectin compared with placebo treatment.
### TABLE 2
Average treatment effects at the 1- and 3-mo assessment corrected for potential baseline differences of placebo, garlic, and atorvastatin treatments on markers of inflammation, endothelial function, and vessel wall activation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo group (n = 26)</th>
<th>Garlic group (n = 28)</th>
<th>Atorvastatin group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>2.74 (0.49–2.44)</td>
<td>3.58 (0.43–10.77)</td>
<td>2.23 (0.25–16.77)</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>46.5 (13.5–110.0)</td>
<td>40.4 (7.99–94.7)</td>
<td>34.0 (10.9–115.0)</td>
</tr>
<tr>
<td>TNF-α after LPS (pg/mL)</td>
<td>211 (99.0–634)</td>
<td>225 (76.8–774)</td>
<td>239 (121–543)</td>
</tr>
<tr>
<td>Von Willebrand factor (%)</td>
<td>5.44 (1.72–13.8)</td>
<td>5.43 (1.55–20.4)</td>
<td>6.37 (2.42–25.1)</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>4.00 (2.85–5.55)</td>
<td>4.10 (2.76–5.30)</td>
<td>3.78 (2.66–5.51)</td>
</tr>
<tr>
<td>s-ICAM (ng/mL)</td>
<td>223 (149–319)</td>
<td>204 (102–398)</td>
<td>199 (132–355)</td>
</tr>
<tr>
<td>s-Selectin (ng/mL)</td>
<td>29.2 (14.0–50.2)</td>
<td>27.8 (12.3–88.9)</td>
<td>30.0 (18.4–68.7)</td>
</tr>
<tr>
<td>s-VCAM (ng/mL)</td>
<td>532 (256–893)</td>
<td>535 (235–761)</td>
<td>590 (315–1345)</td>
</tr>
<tr>
<td>% Change (97.5% CI of difference)</td>
<td>17.8 (−5.0–46.0)</td>
<td>22.9 (−45.3–8.8)</td>
<td>26.6 (−17.9–95.1)</td>
</tr>
<tr>
<td>P</td>
<td>0.0158</td>
<td>0.0016</td>
<td>0.001</td>
</tr>
</tbody>
</table>

### TABLE 3
Average treatment effects at the 1- and 3-mo assessment corrected for potential baseline differences of placebo, garlic, and atorvastatin treatments on lipid and lipoprotein variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo group (n = 26)</th>
<th>Garlic group (n = 28)</th>
<th>Atorvastatin group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>5.58 (4.13–8.26)</td>
<td>5.47 (4.08–7.72)</td>
<td>5.37 (3.92–8.22)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.22 (0.71–2.47)</td>
<td>1.27 (0.64–1.87)</td>
<td>1.13 (0.79–2.20)</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.33 (2.20–6.11)</td>
<td>3.37 (2.06–6.54)</td>
<td>3.23 (2.04–5.86)</td>
</tr>
<tr>
<td>Triacylglycerol (mmol/L)</td>
<td>1.39 (0.64–4.12)</td>
<td>1.56 (0.83–6.11)</td>
<td>1.53 (0.52–6.40)</td>
</tr>
<tr>
<td>% Change (97.5% CI of difference)</td>
<td>0.9 (−5.5–7.8)</td>
<td>1.3 (−8.3–12.0)</td>
<td>−2.8 (−17.1–13.9)</td>
</tr>
<tr>
<td>P</td>
<td>0.7516</td>
<td>0.363</td>
<td>0.6795</td>
</tr>
</tbody>
</table>

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1. TNF-α, tumor necrosis factor; LPS, lipopolysaccharide; s-ICAM, soluble intercellular adhesion molecule; s-VCAM, soluble vascular cell adhesion molecule.
2. There were no significant differences among the groups at baseline, P < 0.05 (ANOVA).
3. Comparisons were analyzed by mixed-model ANOVA with baseline as the covariate; 97.5% CIs to correct for multiple comparisons.
4. Contrasts were not reported for variables with nonsignificant treatment-within-time effects.

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2. Comparisons were analyzed by mixed-model ANOVA with baseline as the covariate; 97.5% CIs to correct for multiple comparisons.
3. Contrasts were not reported for variables with nonsignificant treatment-within-time effects.
Lipids and lipoproteins

Garlic treatment did not influence the total cholesterol, HDL-cholesterol, LDL-cholesterol, and triacylglycerol concentrations when compared with placebo treatment. In contrast, atorvastatin treatment resulted in lower concentrations of total cholesterol (37.2%; 97.5% CI: 33.1%, 41.1%), LDL cholesterol (52.7%; 97.5% CI: 47.9%, 57.1%), and triacylglycerols (31.9%; 97.5% CI: 20.8%, 41.5%) when compared with placebo treatment. HDL-cholesterol concentrations were not significantly affected by atorvastatin (P = 0.34; Table 3).

DISCUSSION

The present placebo-controlled study investigated the effects of a 12-wk treatment intervention with a chemically well-characterized and production-controlled garlic powder in subjects with known risk factors for CVD. A group receiving atorvastatin was used as positive control. The study aimed to identify the effects of garlic powder on inflammatory markers (in particular CRP), endothelial function, and measures of lipid metabolism. The main finding of the study is that garlic powder has no detectable effects on CRP, TNF-α, in the basal and stimulated state or lipid concentrations, whereas these concentrations were positively affected by atorvastatin. This makes it unlikely that garlic exerts a beneficial effect on CVD by antiinflammatory or lipid-lowering mechanisms.

The emphasis on the potential antiinflammatory effects of garlic was chosen because of the observations of in vitro studies which showed that high concentrations of garlic decreased cytokine production in endothelial cells which in turn suggested distinct antiinflammatory properties (20, 21, 28). In addition, a growing body of evidence suggests that inflammatory processes play an important role in the pathophysiology of atherosclerosis. Because it has been shown that CRP is one of the strongest predictors for the risk of atherosclerosis and cardiovascular events in subjects with and without CVD (16–18), this marker was chosen as primary endpoint in the current study. Note that our study had an a priori power of 70–80% to detect a 25–30% decrease in plasma CRP concentration. This percentage decrease was considered relevant because other studies have shown similar effects of atorvastatin on CRP (26). Because our study population had a relatively high mean plasma concentration of CRP (2 mg/L) when compared with healthy volunteers (0.3 mg/L), it can be argued that the results obtained in our population might not be representative for patients with a higher risk of CVD. Instead, our population had only 2 known risk factors (overweight and smoking) for CVD, and the participants were normotensive and normcholesterolemic. We feel, however, that the choice for this population is justified. First, it may be considered unethical to perform a similar study in patients with overt hypercholesterolemia because indicated medical treatments for these conditions are available. Second, it has been shown that elevated CRP concentrations as observed in our population are an independent risk factor for CVD. Finally, it has been shown that effective treatments have a CRP- and lipid-lowering effect in overweight subjects (22) and even in healthy volunteers (23). Thus, by choosing this population with not readily amendable risk factors for CVD a relevant population was studied.

The relatively high garlic dose administered in the present study was chosen because there are some indications that higher garlic doses are associated with greater effects. Indeed, previous studies that showed no beneficial effects of garlic on lipid metabolism and blood pressure in humans used garlic powder doses that varied from 0.3 g/d to 1 g/d (9–13) for which it may be argued that the garlic dose was too low. Therefore, in the present study, we choose a relatively high dose of the garlic powder (2.1 g/d, approximately equivalent to 9.4 mg allicin/d or 5.2 g fresh garlic/d) to be able to detect potentially beneficial effects of garlic powder. Furthermore, a pharmaceutical formulation was used that complies with all requirements for optimal release and bioavailability of the supposedly active compounds of garlic (25, 29).

The compliance data suggested that the adherence to the dosing regimens was good. Obviously, measurement of garlic components and atorvastatin plasma concentrations could have corroborated this observation, but, unfortunately, these data were not available. The effects of atorvastatin were as expected, supporting the notion that compliance was good, at least in the positive control group.

Apart from the primary endpoint, other markers of inflammation (fibrinogen and leukocyte TNF-α production in response to lipopolysaccharide), our data show that garlic powder had no significant effects on any of these markers, whereas atorvastatin showed antiinflammatory effects also on TNF-α concentrations. This suggests that garlic has no significant effect on the inflammatory processes associated with atherosclerosis.

For a long time the lipid- and lipoprotein-lowering properties of garlic have been raised as a mechanism by which garlic could exert a beneficial effect on atherogenesis, although this is not unambiguously supported. Our data appear to be in keeping with the latter findings because we did not observe any effect of garlic on plasma lipids and lipoproteins. In contrast, atorvastatin treatment significantly decreased total cholesterol, LDL-cholesterol, and triacylglycerol concentrations. A posteriori power analysis with the data obtained in the present study indicated that the study had a power of 80% at a 2-sided level, P = 0.05, to detect a decrease of 0.95 mmol/L in total cholesterol concentration (a 17% decrease).

In conclusion, our data showed that 12 wk of treatment with a high-dose, chemically well-characterized, production-controlled garlic powder had no antiinflammatory or lipid-lowering effect in a normolipidemic population with known risk factors for CVD. As such, we conclude that evidence does not show that the garlic powder Printanor that was specially selected and optimally pharmaceutically formulated has beneficial effects on atherogenesis and, consequently, cardiovascular events in a relevant population through antiinflammatory processes or lipid-lowering effects. The findings of the present study lead us to speculate that garlic powder (and probably garlic in general) has no relevant place in the prevention or treatment of the inflammatory and dyslipidemic features of atherosclerosis.

We thank all the people involved in the European Union project Garlic and Health for their collaboration.

SMES analyzed the data and wrote the manuscript; MBAvD executed the study, analyzed the data, and wrote the manuscript; PM, VD, and AV performed the laboratory assays; IMK wrote the protocol and executed the study; RCS developed the protocol, analyzed the statistics, and wrote the manuscript; TH developed the garlic and garlic-placebo formulations; RG performed the study setup; AFC developed the protocol, executed the study, and
reviewed the manuscript; HMP developed the protocol, supervised the laboratory assays, and reviewed the manuscript; JB developed the protocol, executed the study, analyzed the data, wrote and reviewed the manuscript and review, and was the principal investigator. SMES and MBAvd contributed equally to the study. TH is an employee of Lichtwehr Pharma AG; none of the other authors had a conflict of interest.

REFERENCES