Effect of dried garlic powder tablets on postprandial increase in pulse wave velocity after a fatty meal: preliminary observations

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Abstract

Background: Garlic and sulfur-containing components of garlic have been reported to stimulate nitric oxide synthesis in the endothelium. Nitric oxide production is an important determinant of arterial stiffness.

Objective: To examine the impact of dried garlic powder tablets on arterial stiffness as assessed by measurements of pulse wave velocity (PWV).

Design: Two separate randomized cross-over studies of healthy people (trial I: $n=13$; trial II: $n=9$) were conducted. On separate days, participants consumed a high-fat meal (50 g fat) supplemented with garlic powder tablets (8.4 mg alliin), and an identical, but unsupplemented meal. PWV (m s^{-1}) was measured immediately before and 2–3 h after the test meal.

Results: The unsupplemented fatty meal resulted in a significant 5–6% postprandial increase in PWV in both trials (I: $+0.19 \text{ m s}^{-1}$, $p=0.04$; II: $+0.21 \text{ m s}^{-1}$, $p=0.02$). In contrast, the supplemented meal was not associated with any postprandial PWV changes in either trial (I: -0.02 m s^{-1} , $p=0.31$; II: 0.00 m s^{-1} , $p=0.95$). In pooled analysis (trials I and II), the inhibitory effect of garlic powder on the fatty meal-induced postprandial PWV increase was statistically significant ($+0.20 \text{ m s}^{-1}$ vs -0.01 m s^{-1} , $p=0.01$).

Conclusions: The postprandial increase in PWV associated with consumption of a high-fat meal seems to be prevented by dried garlic powder supplementation. Larger, blinded and placebo-controlled trials are needed to confirm the possible antiatherogenic effect.

Keywords: *alliin; arterial compliance; arterial stiffness; atherosclerosis; coronary heart disease; nitric oxide*

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Introduction

It has been reported that garlic may delay the atherosclerotic process (1), and earlier studies supported the theory that garlic supplements lowered cholesterol. However, recent controlled studies were not able to confirm the cholesterol-lowering effect of garlic preparations (2, 3). Any possible effect on atherosclerosis may thus be mediated through alternative mechanisms.

Atherosclerosis is associated with a decreased release of nitric oxide (NO) from the arterial endothelium (4, 5). Aqueous extracts of garlic have been reported to stimulate NO production in human platelets *in vitro* (6) and in living mice (7). NO is an important *in vivo* arterial vasodilator in

humans (4). If active substances present in garlic also affect *in vivo* NO production in the human arterial endothelium, garlic consumption might be associated with improved arterial compliance, i.e. decreased arterial stiffness.

Garlic contains a wide spectrum of sulfur-containing substances. In the present trials dried garlic powder was used as the study supplement. Dried garlic powder tablets are very similar to fresh garlic with respect to chemical components (8). Like intact garlic cloves, dried garlic powder contains alliin, the inactive precursor of the biologically highly potent and strongly smelling allicin. The conversion of alliin to allicin solely depends on an enzyme, alliinase, which is present in fresh garlic as well as

in the dried garlic powder tablets. Alliinase is not released from the dried garlic tablets until the tablets are dissolved in the gastrointestinal tract.

Earlier studies showed that high-fat meals cause increased arterial stiffness in the first postprandial hours (9, 10). The present trials tested whether dried garlic powder supplementation of fatty meals could limit or inhibit this postprandial increase in arterial stiffness. Arterial stiffness was assessed by measurements of pulse wave velocity (PWV) (11).

Material and methods

Two separate randomized, cross-over studies (trials I and II) with slightly different designs were conducted. Trial I comprised 13 people (eight men and five women), with a mean age of 33.4 years (SD 11.9) and a mean body mass index (BMI) of 23.5 kg m^{-2} (SD 2.5). Once the surprising results of trial I were known, the decision was made to perform trial II a few months later to see whether the results of trial I could be confirmed with the use of an alternative garlic powder source. Trial II included nine female students with a mean age of 27.4 years (SD 1.8) and a mean BMI of 22.7 kg m^{-2} (SD 3.4). It was conducted within the framework of a teaching programme and therefore had to be designed slightly differently to trial I.

All volunteers were healthy and were employed or studying at The Royal Veterinary and Agricultural University, Frederiksberg, Denmark. All participants were normotensive ($<135 \text{ mmHg}$ systolic and 90 mmHg diastolic blood pressure). None was a regular user of medications, apart from oral contraceptives (I: $n=2$; II: $n=3$). Two were light smokers (5 cigarettes day^{-1}). The trials were approved by the local ethics committee (file no. KF 01-071/99). Informed consent was obtained from all participants.

The subjects were given the same high-fat meal [3.8 MJ, 50.1 g fat (30.2 g saturated fatty acids, 12.5 g monounsaturated fatty acids, 2.6 g polyunsaturated fatty acids), 35.0 g protein, 78.5 g carbohydrate] consisting of white bread, butter, cheese and full-fat milk on two separate days. The duration between the two study days varied from 2 to 23 days. On one of the two days, the meal was randomly supplemented with garlic powder tablets (I: Kwai[®], Lichtwer Pharma, Berlin, Germany; II: Futura[®], Dansk Droge, Ishøj, Denmark; I and II: alliin dose = 8.4 mg). In trial I, seven subjects had their first meal supplemented with tablets. In trial II,

four subjects had their first meal supplemented. In trial I, participants consumed the test meal between 09.00 and 11.00 h, after at least 10 h of fasting. In trial II, the meal was consumed between 13.00 and 15.00 h, after at least 4 h of fasting. Subjects were asked not to change dietary and physical activity habits during the study period. On test days, participants were not allowed to smoke or to consume drinks or food apart from the test meals served until all measurements had been taken.

PWV was determined in the arterial segment between aorta ascendens and arteria radialis. The pulse transit time from the aortic root to arteria radialis was assessed as the average of 20 consecutive measurements of the time difference between the R-peak of the QRS-complex of the electrocardiogram and the arrival of the pulse (i.e. the steep initial rise of the pulse wave) at the wrist as recorded by an infrared light probe. The sampling and calculation of the mean transit time were computerized (Pulse 4.0; MRC Environmental Epidemiology Unit, Southampton University, UK). After automatic, or if necessary, manual marking of the relevant points, the mean transit time was computed with a computer program (Pulse Analysis Program v97.1.1; LM Styles, Southampton University, UK). PWV (m s^{-1}) was calculated as the distance from the sternal notch to the light probe position (measured by a tape measure on the surface of the body) divided by the mean transit time. PWV data were collected just before and again in the post-absorptive phase 2–3 h after the test meal (identical time schedule on both test days for each individual). All PWV data analyses were undertaken several days later by an investigator blinded to treatment assignments.

All statistical analyses were performed using SPSS for Windows, version 9.0 (SPSS, Chicago, IL, USA). The Student's paired *t*-test was used for normally distributed data, whereas the Wilcoxon Signed Ranked Test was used for data that were not normally distributed. Significance levels were two-sided. The significance level was set at $p < 0.05$ (two-sided). Data from the two trials were pooled testing the effect of garlic, meal order (AB or BA), trial number (I or II) and interaction of trial number $\times$ garlic in a univariate general linear model. The effect of meal order, trial number and interaction of trial number $\times$ garlic were all found to be insignificant. Consequently, it was inferred that

the effect of garlic was comparable in the two trials, and that it was justified to pool data from the two trials in one model.

Results

Trial I

Mean PWV was 3.56 m s^{-1} (SEM 0.14) before the unsupplemented meal and 3.57 m s^{-1} (SEM 0.09) before the supplemented meal (non-significant difference). Mean PWV increased from 3.56 to 3.75 m s^{-1} (SEM 0.14) with the unsupplemented meal ($p=0.04$), whereas mean PWV was virtually unaffected by the supplemented meal [changed from 3.57 to 3.55 m s^{-1} (SEM 0.12), $p=0.31$]. The 0.19 m s^{-1} PWV increase with the unsupplemented meal was not significantly different from the 0.02 m s^{-1} PWV decline observed with the supplemented meal ($p=0.12$) (Fig. 1).

Trial II

Mean PWV was 3.77 m s^{-1} (SEM 0.12) before the unsupplemented meal and 3.87 m s^{-1} (SEM 0.17) before the supplemented meal (non-significant difference). Mean PWV increased from 3.77 to 3.98 m s^{-1} (SEM 0.11) with the unsupplemented meal ($p=0.02$), but was unaffected by the supplemented meal [postprandial mean PWV 3.87 m s^{-1} (SEM 0.14), p for change = 0.95]. The 0.21 m s^{-1} PWV increase with the unsupplemented meal was not significantly different from no change as seen with the supplemented meal ($p=0.12$) (Fig. 1).

After pooling data from the two trials, postprandial PWV changes differed significantly between unsupplemented and supplemented meals [$+0.20 \text{ m s}^{-1}$ (SEM 0.06) vs -0.01 m s^{-1} (SEM 0.07), $p=0.01$].

No significant effects on blood pressure or heart rate were observed in either of the trials (Tables 1, 2).

Fig. 1. Individual pulse wave velocity (PWV, m s^{-1}) before and 2–3 h after consumption of an unsupplemented and a dried garlic-supplemented fatty meal (fat content: 50 g) served on separate days in a cross-over design in two separate trials: I ($n=13$) and II ($n=9$).

Table 1. Trial I: values of systolic and diastolic blood pressure and heart rate before and 2–3 h after a fatty meal (50 g) with and without garlic powder tablets (8.4 mg alliin) (cross-over study)

		Fat+garlic (n = 13)	Fat (n = 13)	p (difference)
Systolic blood pressure (mmHg)	Before	111.8 (106.0–117.5)	112.8 (107.0–118.6)	0.51
	After	113.2 (108.3–118.2)	112.2 (105.9–118.4)	0.54
	Change	1.5 (–1.2 to 4.1) $p = 0.25$	–0.6 (–4.5 to 3.3) $p = 0.74$	0.33
Diastolic blood pressure (mmHg)	Before	70.2 (67.1–73.2)	69.3 (66.5–72.0)	0.31
	After	66.6 (64.3–69.0)	66.2 (63.5–68.9)	0.62
	Change	–3.5 (–5.6 to –1.5) $p = 0.003^{**}$	–3.1 (–5.3 to –0.9) $p = 0.01^*$	0.69
Heart rate	Before	58.1 (54.1–62.1)	58.8 (54.9–62.7)	0.75
	After	61.5 (56.8–66.3)	59.9 (56.2–63.5)	0.36
	Change	3.5 (–0.2 to 7.1) $p = 0.06$	1.1 (–1.5 to 3.7) $p = 0.38$	0.27

Data are means and 95% confidence intervals. Change was tested with the Student's *t*-test.

Postprandial value significantly different from preprandial value: $^{**}p < 0.01$, $^*p < 0.05$.

Discussion

In each of the two separate trials, consumption of the unsupplemented fatty meal was associated with a significant 5–6% increase in PWV, whereas garlic powder supplementation of the meal inhibited the postprandial PWV increase. Owing to insufficient statistical power, the effect of garlic powder was not statistically significant in the individual trials. However, in the pooled statistical analysis of data from both trials, the garlic powder effect became significant. The pooling of data was justified by analyses demonstrating that the effect of garlic powder did not differ significantly between the

two trials (for details see Material and Methods, last paragraph).

An increase in PWV reflects a more rigid vessel, i.e. a stiffening of the investigated arterial segment, provided blood pressure does not change. No blood pressure changes were observed, and this finding is thus in line with earlier studies where fatty meals containing around 50 g fat were shown to cause a postprandial increase in arterial stiffness (9, 10).

The arterial stiffness is determined by the relative presence of elastin and collagen in the arterial wall, the presence of atherosclerosis and the arterial smooth muscle tone. Only the vascular tone is

Table 2. Trial II: values of systolic and diastolic blood pressure and heart rate before and 2–3 h after a fatty meal (50 g) with and without garlic powder tablets (8.4 mg alliin) (cross-over study)

		Fat+garlic (n = 9)	Fat (n = 9)	p (difference)
Systolic blood pressure (mmHg)	Before	113.9 (103.9–124.0)	112.4 (104.8–120.0)	0.26
	After	109.8 (101.4–118.3)	110.6 (104.2–117.0)	0.75
	Change	–4.1 (–7.9 to –0.4) $p = 0.04^*$	–1.9 (–4.6 to 0.8) $p = 0.14$	0.31
Diastolic blood pressure (mmHg)	Before	72.1 (66.4–77.7)	71.1 (65.8–76.3)	0.04
	After	67.9 (64.2–71.7)	67.4 (64.5–70.3)	0.39
	Change	–4.1 (–7.8 to –0.5) $p = 0.03^*$	–3.6 (–7.2 to –0.0) $p = 0.05^*$	0.50
Heart rate	Before	68.0 (63.5–72.5)	64.0 (57.7–70.3) ^a	0.10
	After	71.4 (65.1–77.6)	69.8 (64.5–75.1)	0.26
	Change	3.4 (–3.4 to 10.2) $p = 0.28$	7.2 (3.1 to 11.2) ^a $p = 0.01^{**}$	0.38

Values are means and 95% confidence intervals. Change was tested with the Student's *t*-test.

Postprandial value significantly different from preprandial value: $^*p < 0.05$, $^{**}p < 0.01$.

^aNumber of participants in whom the parameters in question were measured ($n = 8$). In all other cases the number is as given at the top of the column.

changeable in short-term studies of hours' duration. The postprandial increase in arterial stiffness with fatty meals therefore has to be explained by a change in vascular tone. The mechanism explaining this phenomenon is unknown, but is probably related to the postprandial occurrence of triglyceride-rich lipoproteins that may influence the endothelial release of vasoactive compounds, including NO (5). The apparent effect of garlic powder on postprandial arterial stiffness may also be mediated by vasoactive compounds. This possibility is supported by studies reporting that garlic products enhance the production of NO (6, 7). Further support comes from two studies reporting that garlic extract and the important sulfur-containing garlic metabolite, allicin, produce an endothelium- and NO-dependent relaxation in rat pulmonary arteries and aorta (12, 13). In line with these observations, cell and animal studies have demonstrated that garlic and certain garlic compounds may increase the activity of constitutive nitric oxide synthase (cNOS) (6, 7, 14), whereas inducible nitric oxide synthase (iNOS) is unaffected or inhibited by garlic/garlic compounds (14, 15). The influence of garlic powder on postprandial arterial stiffness could also be explained by alternative mechanisms. Garlic powder may modify the postprandial lipid metabolism or have antioxidant properties. At least one earlier trial has demonstrated that certain antioxidants may acutely affect arterial compliance (16).

The two trials reported here had slightly different designs, but their results were remarkably similar and not statistically distinguishable (as described above). There was a 6–8% difference in baseline PWV between the two study groups, which may be partially explained by differences in the characteristics of the participants. It is known that PWV is influenced by, among other things, gender, age and hormone therapy (17–19). The fasting period before test meal consumption varied between trial I (10 h) and II (4 h), and this may also have contributed to the difference in baseline PWV, as well as possible diurnal variations.

Both trials were randomized and had a cross-over design. Possible biases caused by differences in gender, age, body weight, diet, smoking habits and the use of hormones can thus be excluded. Although both trials included an active and a control treatment, they were both open and did not include the use of placebo tablets. Investigator-

related biases cannot therefore be excluded. However, it should be noted that the PWV data collection was computerized, except for the measurement of the length of the arterial segment.

In conclusion, this study suggests that the postprandial increase in PWV associated with consumption of a high-fat meal may be prevented by dried garlic powder supplementation. This observation may be explained by an effect of garlic compounds on the endothelial release of NO. Larger, blinded and placebo-controlled studies are needed to confirm the present preliminary observations of this possibly antiatherogenic effect of dried garlic powder.

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