Effects of Garlic Oil on Platelet Aggregation, Serum Lipids and Blood Pressure in Humans[1,2]

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Abstract

The effect of oral ingestion of garlic oil was studied in 20 healthy human volunteers in a double-blind, two period, cross-over trial. The individuals were randomly divided into two groups. Each group rotated for four week periods through 2 different sequences of oral supplementation including: 18 mg of garlic oil (extracted from 9 grams of fresh garlic) and placebo. The amount of platelet aggregation decreased significantly ($p < .005$) during garlic administration. Serum cholesterol levels and mean blood pressure both decreased significantly ($p<.011$, $p<.009$) during garlic supplementation. Serum high density lipoprotein levels rose significantly ($p.<.001$) during garlic administration. There was a significant rise in arachidonic acid in red cell phospholipids following garlic administration. The results of this study (the first double-blind, crossover study) suggest that garlic has therapeutic potential as an anti-atherosclerotic, antithrombotic and anti-hypertensive agent in normal healthy adults.

Garlic, known botanically as *Allium sativum, is* a widely distributed common plant. It is used in all parts of the world not only as a spice and food, but also as a popular folk remedy for a variety of ailments. Its importance had been recognized several thousand years ago in China, India and Egypt. In 1944 the essential oil, believed to be the active ingredient, was distilled out and named Allicin . There recently has been renewed research in the therapeutic uses of garlic. Hypolipidemic[2-13], platelet aggregation inhibition[14-18], antiatherosclerotic[10-24] fibrinolytic enhancement[25,26], anti-bacterial and anti-fungal[27] properties have all been reported.

Atherosclerosis and coronary artery disease remain the number one killers in civilized countries of the world. It is now recognized that hyperlipidemia is associated with increased incidence of premature ischemic heart disease[28]. Hypercholesterolemia correlates highly with the risk of myocardial infarction[29]. Elevated high density lipoprotein (HDL) levels may exert a protective effect against coronary artery disease[30].

Due to the previously reported positive effect of garlic on these blood components in unblinded tests on animals and humans, this study was designed to test some of these parameters in a controlled double-blind study with normal human volunteers.

Methods

Twenty student volunteers, average 26 years of age, enrolled in the project. All completed informed consent letters and the project was approved by the Human Subjects Review Committee of the College. All were in good health and showed no signs of degenerative cardiovascular disease. Each person was given a list of drugs that affected platelet aggregation and was asked to avoid these during the trial. Individuals were also asked to limit dietary garlic. No other dietary restrictions were imposed.

The design of the study was a double-blind, two-period crossover trial. The individuals were randomly divided into 2 groups.

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Each group rotated through the following four-week supplementation periods: 18 mg of cold pressed garlic oil (extracted from 9 g of fresh garlic) per day; and placebo. The active regime perles also contained 158 mg coconut oil, 30 mg glycerin and 54 mg gelatin. The placebo perles contained 160 mg coconut oil, 30 mg glycerin and 54 mg gelatin. The placebo perle bottles (containing 60 capsules) were laced with 500 mcg of garlic oil. Both the active and placebo bottles had strong garlic odors. There was a three week wash-out period between each four week supplementation period during which no capsules were taken. Capsules were taken with meals. The supplements were formulated and coded by General Nutrition Research Laboratories, Fargo, North Dakota.

Platelet aggregation percentages, serum lipid levels and blood pressure readings were measured before and after each supplementation period. Fasting (6 h) blood samples were obtained by venipuncture from the antecubetal fossa using a 10cc vacutainer (BD 6430).

Five cc of blood were transferred to a plastic tube containing 3.8% sodium citrate, incubated at 37^0C for 30 m and then spun at slow speed, with 500 ul extracted as platelet rich sample; the remainder was spun at high speed for platelet poor sample. Using a Chronolog Aggregometer (#430) and an experimental Chronolog Whole Blood Aggregometer for comparison, agglutination times were measured after exposure to ADP.[31]

The remaining 5 cc of blood was allowed to clot and then spun at high speed with the serum being removed and subject to direct quantitative colorimetric determination of total and HDL cholesterol levels using the modified Lieberman-Burchard reaction procedures[32] and a Baush & Lomb Spectomic 21 spectrophotometer.

Individual mean bilateral sitting brachial blood pressures were measured by an experienced technician after each blood sample was drawn.

Participants were asked to refrain from any strenuous exercise for 4 h prior to sampling.

Paired t tests for pairs and class were used to identify statistically significant differences between mean values of changes and differences in change. Students t test was calculated using the computer program

'Statistical Package for the Social Sciences'.

Results

Cholesterol, HDL, mean blood pressure levels and platelet aggregation percent after supplementation with placebo and with garlic are presented in Table 1. During garlic administration, platelet aggregation was reduced significantly, by 16.4% ($p < .005$) as compared to no significant change during placebo administration (between classes with no cross-over).

Figure 1 illustrates the change in mean cholesterol levels during the two different supplementation periods. Mean serum cholesterol levels dropped significantly (from 195 to 180 mg/100 ml, $p < .001$) during garlic administration. There was a slight insignificant drop during placebo trial. The difference in change during the garlic versus placebo administration was also significant (12.5 mg/100 ml, $p<.01$).

Results from HDL measurements are presented in Figure 2. Mean HDL levels rose significantly during garlic supplementation (from 56 to 69 mg/ 100ml, $p< .001$). The difference in change between the two periods was also significant (8.3 mg/100ml, $p< .01$). There was an insignificant rise in the HDL levels during placebo trial.

Figure 3 shows the mean blood pressure measurements during each period. Levels dropped significantly during garlic administration (94 to 88 mm HG, $p < .009$). The difference in change between the two supplementation periods was also significant (3 mm HG, $p < .07$). There was a small insignificant drop during placebo trial.

Discussion

Garlic contains an essential oil, allicin ($C_6H_{10}S_{20}$), which contains allylpropyl-disulphide, diallyldisulphide and several other sulphur compounds. The active principal of garlic appears to be the essential oil. The concentration of essential oil in garlic is 0.3 to 0.4%.

In our study garlic administration has led to significant decreases in platelet aggregation, serum cholesterol, mean blood pressure as well as a significant rise in serum HDL's in normal healthy humans when compared to placebo supplementation. Due to the odoriferous nature of garlic oil, no double blind studies have been previously reported. We feel a measure of the success of our novel

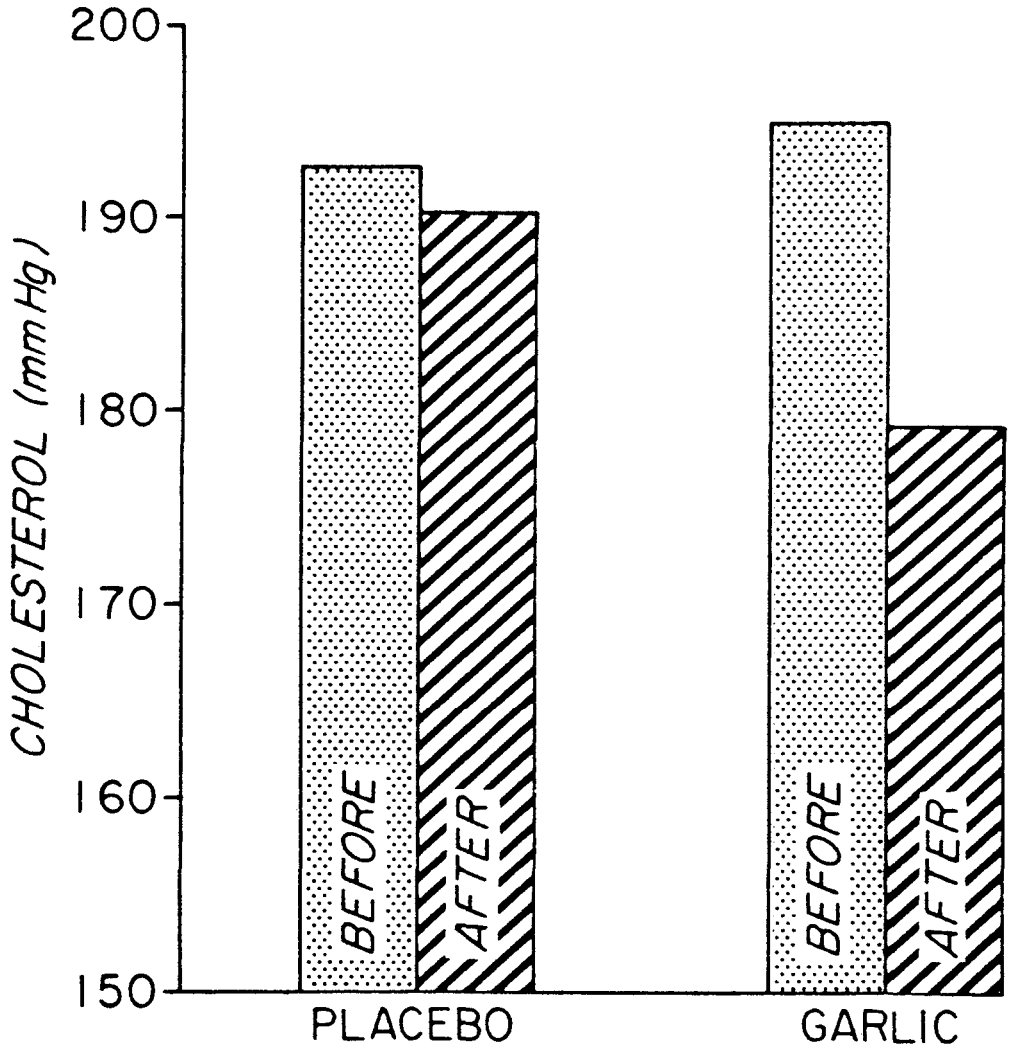

FIGURE 1

Changes in mean cholesterol levels during supplementation with placebo and garlic oil.

'blinding' is the small, but insignificant placebo changes in the same direction as the active trial.

Previous work by Makheja et al[33] has shown garlic extract to inhibit platelet aggregation *in vitro.* The results of their work indicate that garlic almost completely suppresses thromboxane B_2 synthesis. Further results indicate that garlic inhibits platelet aggregation by alterations in both the platelet cyclooxygenase and lipoxygenase pathway. Studies by Ariga et al[34] have isolated this component as methyl allyl trisulphide (MATS) which is a minor component in garlic oil. Bordia[17] has shown that *in vitro* platelet aggregation was markedly inhibited in a dose-related manner when human blood was exposed to garlic oil. Bordia has also shown that oral administration of 25 mgs of garlic for 5 days significantly inhibited platelet aggregation in humans and may inhibit some aspects of thrombus formation. Boullin[35] has reported that eating 10 grams of garlic cloves significantly inhibited platelet aggregation in 3 human volunteers. Work by Apitz-Castro et al[36] suggests that garlic's inhibitory effect might be mediated through modification of the physiochemical properties of the plasma membrane, rather than by affecting the arachidonic or calcium metabolism of platelets.

We also measured the full range of fatty acids in plasma, and red blood cell total phospholipids were measured in order to monitor the possibility that garlic might affect levels of polyunsaturated fatty acids known to influence platelet aggregation. There were no significant changes in plasma

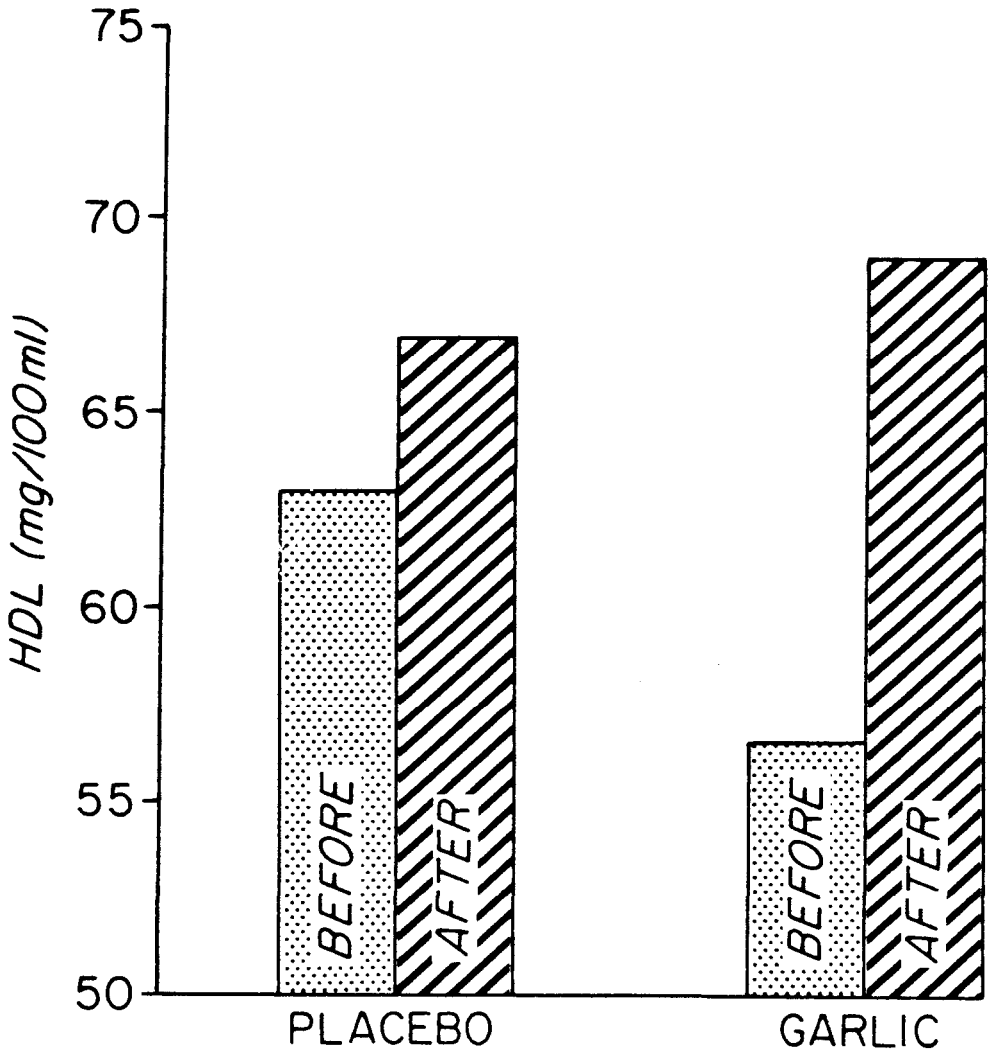

FIGURE 2 Changes in mean HDL levels during supplementation with placebo and garlic oil.

or red cell fatty acids in the placebo group or in plasma fatty acids in the garlic group. There was however, a significant rise in arachidonic acid in red cell phospholipids following garlic administration. This might be consistent with reduced conversion of arachidonic acid to thromboxane A_2, a mechanism of garlic action which has been proposed elsewhere.

This study provides the first support for these previous findings in healthy adults using a controlled double-blind two-period crossover trial.

Previous research examining the effect of garlic on blood lipids in rats, rabbits and humans has been extensive. In cholesterol-fed rats, Chi et al[2] found that garlic feeding increased the excretion of neutral and acidic steroids and exerted a hypocholesterolemic effect. Kamanna et al[9] showed that garlic perles produced a significant decrease in serum and liver cholesterol levels in rats fed an atherogenic diet. Interestingly, Kamanna compared and calculated the efficacy of garlic perles (containing the volatile oil) as being 6 times greater than that of garlic powder. Jain and Konar[8] demonstrated similar results when they fed rabbits an atherogenic diet and observed that garlic oil decreased tissue cholesterol and minimized atheromatous changes in the rabbit aorta. They hypothesize that the low ester cholesterol (EC) value found in the garlic-fed rabbits contributed to the low EC that was found in the vessel intima. Bordia and his coworkers[7] suggest that the protective action of garlic against induced atherosclerosis in rabbits is due to several factors; the restriction of

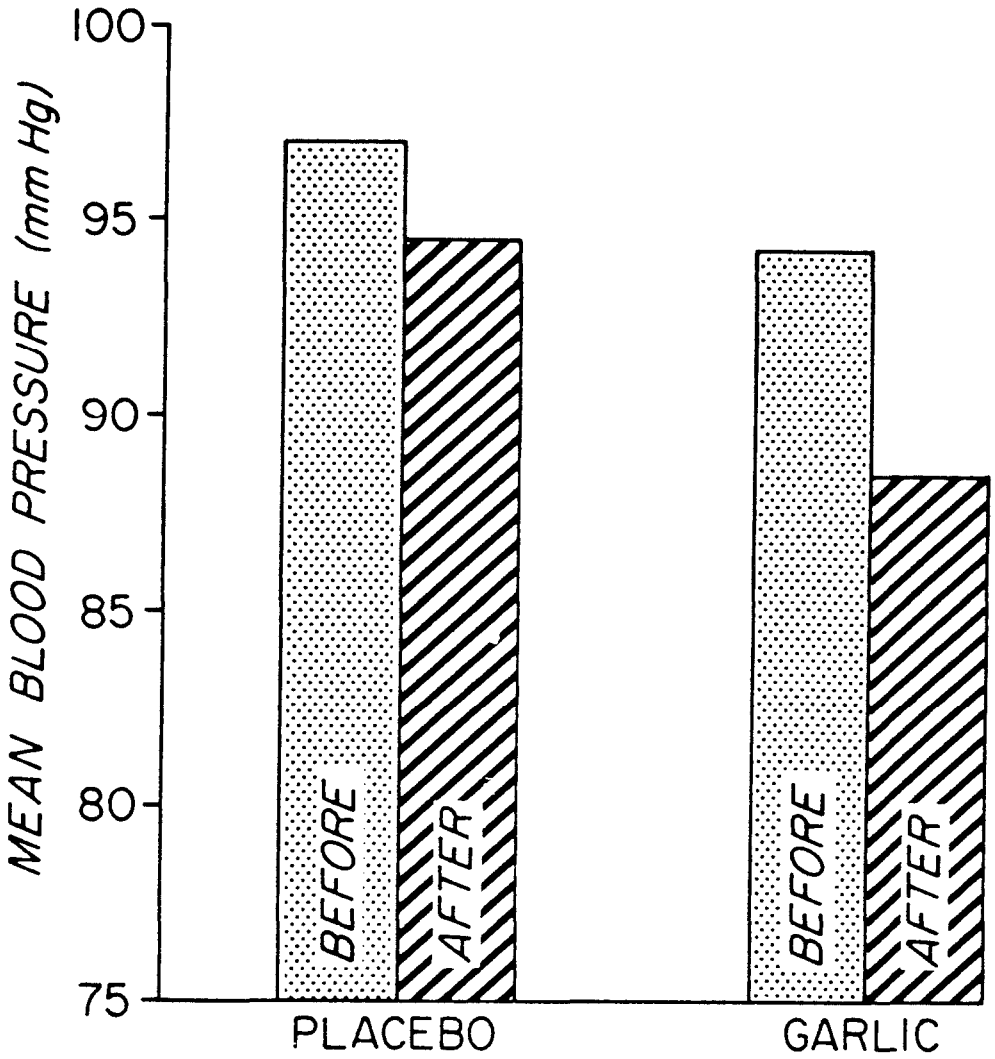

FIGURE 3 Changes in mean blood pressure during supplementation with placebo and garlic oil.

the rise in blood cholesterol and lipids; the minimization of the fall in alpha lipoproteins; and the increased fibrinolytic activity of plasma. In humans, the effect of garlic has been studied in induced alimentary hyperlipidemia, in hypercholesterolemic persons, and in normals. In two separate studies, Bordia and co-workers[4,10] showed that the essential oil of garlic can prevent the harmful effects of fatty meals on humans by preventing the fall in fibrinolytic activity, the rise in serum triglycerides and the rise in the platelet adhesive index normally associated with this type of diet. Bordia[13] also found that in healthy humans fed garlic for six months, serum cholesterol and triglycerides were reduced and HDL levels raised. Augusti[5] hypothesizes that these effects of garlic may be due to allicin lowering the amount of reduced NAD and NADP in the body. Allicin can combine with -SH groups, the functional part of CoA, a necessary part of the biosynthesis of cholesterol. The effect of raw garlic on normal blood cholesterol in humans was studied by Bhusan et al[37]. They found that blood levels decreased significantly in all the participants after two months of garlic ingestion.

Our results parallel those studies reported above. Serum cholesterol levels (initial range from 130 to 270 mg/100 ml) were lowered, and HDL levels (initial range 41 to 94 mg/100 ml) were raised significantly in humans during our blinded trail.

Using spontaneously hypertensive rats, Foushee and Ruffin[38] have reported that 0.5 ml/kg of garlic oil lowered the systolic blood pressure to a normal level and sustained the

TABLE 1

Effect of garlic and placebo on serum cholesterol, serum HDL, mean blood pressure and platelet aggregation.

Measure	Placebo		Garlic		Difference Between
	Beginning	End	Beginning	End	Placebo & Garlic
Cholesterol (mg/100ml)	192.95	190.4	195	179.95	
Period change	-2.55		-15.05*		12.5**
SEM	8.2	8.4	6.8	7.1	
HDL (mg/100ml)	63	67.25	56.45	69	
Period change	4.25		12.55*		8.3**
SEM	2.9	3.7	2.3	2.8	
Blood Pressure (mm/HG)	96.9	94.6	94.2	88.7	
Period change	-2.3		- 5.4**		3.1***
SEM	1.2	1.5	2.2	1.4	
Platelet Agg (% change)	+5.6		-16.4****		

Values presented as Mean + /- SEM (n = 20)
* Significant change (p<.001) *** Significant change (p <. 07) ** Significant change (p < .01) **** Significant change (p < .005)

decrease for up to 24 h. We have found that administration of garlic oil to normotensive humans (mean blood pressure range from 88 to 108 mm HG) for four weeks significantly reduced the mean blood pressure.

The results of this study suggest that garlic oil could be an effective therapeutic agent, as part of a regime for the control and prevention of atherosclerosis and coronary artery disease in humans due to the observed lowering of cholesterol, blood pressure and platelet aggregation. More work still needs to be done in order to better understand its methods of actions.

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