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PRELIMINARY REPORT

Serum Plant Sterols as a Potential Risk Factor for Coronary Heart Disease

Thomas Sudhop, Britta M. Gottwald, and Klaus von Bergmann

In patients with the inherited disease of phytosterolemia, elevated concentrations of plant sterols (eg, campesterol and sitosterol) have been implicated as a risk factor for premature atherosclerosis. Whether plasma concentrations of campesterol and sitosterol are risk factors for coronary heart disease (CHD) in nonphytosterolemia subjects has not been established. Therefore, the present study examined the role of plant sterols in patients admitted for elective artery coronary bypass graft (ACBG). Serum concentrations of campesterol and sitosterol, as well as lathosterol, desmosterol, cholestanol, and lipoproteins were analyzed in 42 men and 11 women without lipid-lowering treatment during the past. Twenty-six patients reported a positive family history in their first-degree relatives for CHD. Lipid profile and other risk factors were comparable in both groups. Patients with a positive family history for CHD had significant higher plasma levels of campesterol (.50 ± .17 *v* .38 ± .16 mg/dL; *P* = .011), sitosterol (.40 ± .11 *v* .31 ± .11 mg/dL; *P* = .004) and their ratios to cholesterol. Lathosterol, desmosterol, cholestanol, and their ratios to cholesterol were not significantly different. Analysis of covariance (ANCOVA) analysis showed no influence of sex, age, triglycerides, total-, low-density lipoprotein (LDL)-, and high-density lipoprotein (HDL)-cholesterol on the results, but confirmed a strong influence of plant sterols. These findings support the hypothesis that plant sterols might be an additional risk factor for CHD.

THE TWO COMMON plant sterols, campesterol and sitosterol, are structurally related to cholesterol. Their presence in diet is almost equal to that of cholesterol, but their absorption rate is markedly lower.[1-3] The important role of elevated plant sterols in humans is illustrated by the inherited disease of phytosterolemia.[4-6] Patients with phytosterolemia have markedly increased plasma concentrations of plant sterols as a result of hyperabsorption and diminished biliary elimination,[3,6,7] which is caused by a defect in either the ABCG5 or ABCG8 transporter genes.[8,9] They develop xanthoma very early and an increased risk of coronary heart disease (CHD) at a young age.[10-12] Glueck et al[13] raised the question whether elevated plant sterols may be a risk factor for CHD in subjects without phytosterolemia. He found that campesterol concentrations in subjects with a family history of CHD are higher than in those without such a history. The present study was thus designed to determine whether patients with proven CHD and a family history of this condition have higher levels of plant sterols compared with those without such a family history.

Patients with CHD admitted to the hospital for elective artery coronary bypass graft (ACBG) operation were asked to participate in the study. Patients taking lipid-lowering drugs during the last 6 weeks or sterol/stanol-enriched products or with recent myocardial infarction were excluded. None of the patients was vegetarian. All participants gave written informed consent. Blood samples and medical history were obtained from 42 men and 11 women aged 46 to 77 years consecutively admitted to the hospital. Blood samples for plasma lipids, cholesterol precursors (lathosterol and desmosterol), and plant sterols (sitosterol and campesterol) were drawn after an overnight fast before surgery. Sterol analysis was performed by gas liquid chromatography. Statistical calculations were computed using Student's *t* tests for independent samples and χ^2 statistics with Yate's correction. Plant sterols were additionally examined in an analysis of covariance (ANCOVA) model to detect possible confounding effects of sex, age, triglycerides, total-, low-density lipoprotein (LDL)-, and high-density lipoprotein (HDL)-cholesterol.

From the Department of Clinical Pharmacology, University of Bonn, Bonn, Germany.

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Address reprint requests to Klaus von Bergmann, MD, Department of Clinical Pharmacology, University of Bonn, Sigmund-Freud-Str 25, 53105 Bonn, Germany.

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Table 1. Serum Lipoproteins, Cholesterol Precursors, and Plant Sterols in Patients With and Without a Positive Family History of Coronary Heart Disease

	Patients Without Family History (n = 27)	Patients With Family History (n = 26)	*P*
Serum lipoproteins			
Total cholesterol (mg/dL)	242 ± 46	242 ± 31	.952
LDL cholesterol (mg/dL)	167 ± 38	169 ± 31	.843
HDL cholesterol (mg/dL)	41 ± 12	39 ± 13	.725
Triglycerides (mg/dL)	171 ± 85	172 ± 98	.988
Cholesterol precursors and cholestanol			
Lathosterol (mg/dL)	0.34 ± 0.15	0.36 ± 0.11	.615
Lathosterol/cholesterol ratio (μg/mg)	1.40 ± 0.53	1.49 ± 0.38	.462
Desmosterol (mg/dL)	0.27 ± 0.13	0.27 ± 0.11	.972
Desmosterol/cholesterol ratio (μg/mg)	1.10 ± 0.49	1.10 ± 0.38	.980
Cholestanol (mg/dL)	0.48 ± 0.16	0.48 ± 0.13	.978
Cholestanol/cholesterol ratio (μg/mg)	1.99 ± 0.65	1.99 ± 0.41	.980
Plant sterols			
Campesterol (mg/dL)	0.38 ± 0.16	0.50 ± 0.17	.011
Campesterol/cholesterol ratio (μg/mg)	1.59 ± 0.61	2.07 ± 0.60	.006
Sitosterol (mg/dL)	0.31 ± 0.11	0.40 ± 0.11	.004
Sitosterol/cholesterol ratio (μg/mg)	1.27 ± 0.46	1.65 ± 0.45	.004

NOTE. Values are mean ± SD.

Twenty-six patients reported CHD in their first-degree relatives (parents or siblings). Twenty-seven patients had no such events in their family history. Sixteen patients with and 9 patients without a positive family history had arterial hypertension ($P = .063$). Diabetes mellitus was present in 6 patients with and 3 patients without a positive family history ($P = .427$). Current or former nicotine abuse was present in 19 and 23 patients, respectively ($P = .455$). Body mass index was also comparable in both groups (25.9 ± 3.0 *v* 26.2 ± 2.7 kg/m^2; $P = .760$). Patients with a family history of CHD had a tendency to be younger at a nonsignificant level (60.9 ± 7.5 *v* 64.0 ± 7.6 years; $P = .139$).

The lipid analysis showed moderate hypercholesterolemia, slightly elevated triglycerides, and LDL-cholesterol, and low HDL-cholesterol concentrations, but no differences between the 2 groups could be detected (Table 1). The LDL- to HDL-cholesterol ratio was comparable ($P = .613$). The concentrations of the cholesterol precursors, lathosterol and desmosterol,

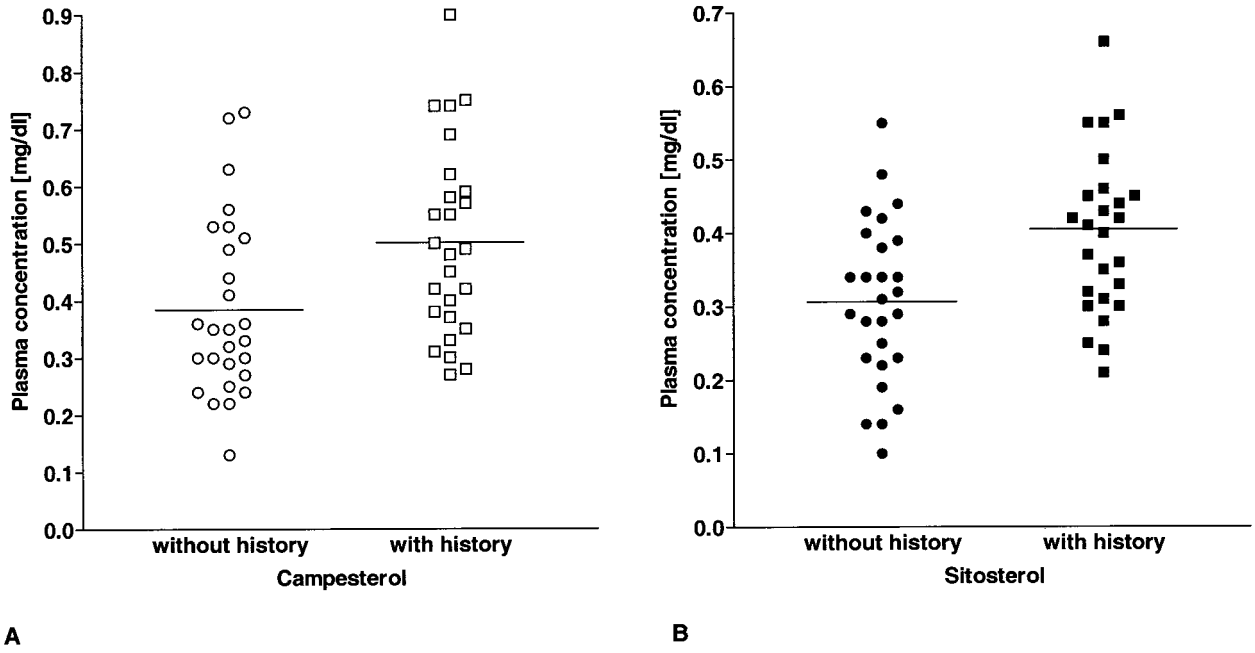

Fig 1. Individual plasma concentrations of the plant sterols (A) campesterol and (B) sitosterol in patients with and without family history of CHD. —, The mean.

and their corresponding ratios to cholesterol did not differ significantly. Plant sterol and lathosterol levels were in the same range as reported in hypercholesterolemic populations from different countries published previously,[14-16] but striking differences between the groups were seen. Serum campesterol and sitosterol concentrations were 30% ($P = .011$) and 29% ($P = .004$) higher in patients with a positive family history compared with those without (Fig 1). These elevations were also confirmed by the ratios of campesterol and sitosterol to cholesterol, while cholestanol plasma concentrations showed no significant differences (Table 1). The ANCOVA analysis showed no confounding effects of sex, age, triglycerides, total-, LDL-, and HDL-cholesterol on plant sterols, but confirmed the dependency on family history.

The present study raises again the question regarding the role of plant sterols as a CHD risk factor as presumed by Glueck et al.[13] Nevertheless, it is not clear whether plant sterols are a risk factor as in phytosterolemia or only a surrogate marker for other mechanisms resulting in an increased risk of CHD. Plasma levels of plant sterols are highly heritable[17] and are a good indicator for the activity the recently discovered ABCG5/8 transporters,[8,9] which regulate, at least in part, intestinal sterol absorption. Thus, the increased plasma concentrations of plant sterols found in patients with a positive family history in the present report might express an increased sterol absorption in these patients resulting in a higher heritable risk of CHD, but more studies are clearly warranted to confirm our preliminary results.

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