Annals of Nutrition & Metabolism

German Vegan Study: Diet, Life-Style Factors, and Cardiovascular Risk Profile

A. Waldmann[a]   J.W. Koschizke[a]   C. Leitzmann[b]   A. Hahn[a]

[a]Institute of Food Science, Centre Applied Chemistry, University of Hannover, Hannover, and
[b]Institute of Nutrition Science, Justus-Liebig-University Giessen, Giessen, Germany

Abstract

Background/Aim: Evaluation of cardiovascular risk profile in 154 German vegans. *Methods:* Cross-sectional study, Germany. Study instruments: 2 FFQ, 2 questionnaires, analyses of fasting venous blood samples. *Results:* The total study population had a low BMI (mean: 22.3 kg/m^2), a moderate blood pressure (mean: 120/75 mm Hg), an extremely low consumption of alcohol (mean: 0.77 g/day) and 96.8% were nonsmokers. Moderate physical activity (PAL) was reported by nearly 50%, whereas 22.7% declared to have a high PAL (>3 h/week). Median triacylglycerol (TG) was 0.81 mmol/l, total cholesterol (TC) was 4.33 mmol/l, HDL was 1.34 mmol/l. The mean TC/HDL-ratio was 3.3. Lipoprotein(a) (Lp(a)) was 8.13 mg/dl, concentrations of >30 mg/dl were prevalent in 25% of the participants. In general, status of folate and pyridoxine were sufficient, while 49.7% showed cobalamin concentrations <150 pmol/l. Plasma homocysteine levels were slightly elevated (median: 12.5 μmol/l). Cobalamin concentration and duration of vegan nutrition were the main determinants of homocysteine in the total study population. *Conclusion:* Although TC and LDL concentrations were favorable, low HDL and elevated homocysteine and Lp(a) concentrations were unfavorable. Overall, these results confirm the notion that a vegan diet is deficient in vitamin B$_{12}$, which may have an unfavorable effect on CHD risk.

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Introduction

Nearly 50% of all deaths in Germany and other industrial countries are related to cardiovascular diseases (CVD) [1]. Most cardiovascular diseases are caused by atherosclerosis, which itself depends upon a multifactorial process, with hypertension, smoking, obesity, and elevated serum low-density lipoprotein concentrations as important associated risk factors [2]. Although it is not yet known whether an elevated homocysteine concentration is a causative factor in the development of atherosclerosis, some authors consider hyperhomocysteinemia to be an important and independent risk factor for cardiovascular diseases [3–6]. To date, no standardized definition of hyperhomocysteinemia exists [7, 8], but experts discuss levels of <10 μmol/l or even lower as being desirable in CVD prevention [9]. Another important risk factor for coronary heart disease (CHD) are increased lipoprotein(a) (Lp(a)) concentrations, which are associated with an approximately 2-fold risk increase for CHD [10–15]. Lp(a) concentrations are mainly genetically determined. However, high therapeutic doses of niacin and hormone replacement therapy are known to have lowering effects on Lp(a) [14, 16].

Prof. Dr. Andreas Hahn
Institut für Lebensmittelwissenschaft, Zentrum für Angewandte Chemie
Abteilung für Ernährungsphysiologie und Humanernährung, Universität Hannover
Wunstorfer Strasse 14, DE–30453 Hannover (Germany)
Tel. +49 511 762 5093, Fax +49 511 762 5729, E-Mail Andreas.Hahn@lw.uni-hannover.de

A broad spectrum of epidemiological data shows that vegetarians have lower CVD related morbidity and mortality [17,18]. While a lacto-ovo vegetarian diet can be recommended in this context, data on the overall CVD risk profile situation of vegans are limited.

The present study aimed at evaluating the cardiovascular risk profile and related dietary and life-style factors in vegans. Participants were classified into strict and moderate vegans in order to investigate whether even a very small amount of ingested food of animal origin may have an impact on risk profile.

Methods

The German Vegan Study (GVS) was designed as a cross-sectional study. Advertisements for subjects were placed in eight German magazines. The GVS was conducted in accordance with the Helsinki Declaration of 1964 as revised 1983 and 1996. Since there was no intervention, the Ethics Commission of Lower Saxony confirmed that ethical approval was not required. All subjects participated voluntarily and gave written consent prior to study begin. Inclusion criteria were defined as: vegan nutrition for one year prior to the beginning of the study, a minimum age of 18 years, no pregnancy or childbirth during the last 12 months. Exclusion criteria were defined as: Severe illness during the last 12 months (such as malignant or cardiovascular diseases, renal failure and severe diseases of the gastrointestinal tract), diagnosed blood coagulation disorder, intake of inhibitors of blood coagulation, misuse of alcohol and/or drugs, participation in another study during the last month.

As previously described [19], participants were classified as vegan when adhering to either a strict vegan diet (SV) or a moderate vegan diet (MV), i.e. a maximum of 5% of the ingested energy was derived from eggs, milk and/or dairy products. On the one hand, the ingested amounts of eggs (0.88 ± 3.31 g/day), milk and dairy products (7.95 ± 10.1 g/day) in the moderate vegan subgroup was so low that it seemed not to be appropriate to name them restricted lacto-ovo-vegetarians. On the other hand, although all persons reported to be vegans, some persons included food of animal origin in their diet. And the consumption of eggs, milk and dairy products makes it difficult – if not impossible at all – to name those persons (strict) vegans. Therefore, we decided to name them moderate vegans rather than restricted lacto-ovo-vegetarians or strict vegans.

Each GVS participant was asked to complete two 9-day estimated food frequency questionnaires (FFQ). The FFQ used was a slight modification (complemented for vegan foods, foods of animal origin (except eggs, butter, milk and dairy products) were excluded) of the validated FFQ used in the Giessen Raw Food Study [20]. Altogether, the GVS-FFQ contained 199 vegan foods (incl. 18 beverages) and 7 non vegan foods (i.e. eggs, milk, and other dairy products). In the FFQ common household measures and their equivalents in grams or milliliters were given for each food item. In some cases, portion sizes were made clear with photos or comments (i.e. 9 walnut-size strawberries weighing 150 g, 1 orange with a size of a tennis ball equals 250 g). In addition, participants were asked for copies of recipes of home made vegan dishes. In order to minimize seasonal differences, one FFQ was sent in autumn, the other in spring. Members of the GVS team developed software (Paradox and Access database) on the basis of the German Nutrient Data Base (BLS II.2, Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin Berlin, Germany) to calculate the concentrations of ingested nutrients.

A short pre-questionnaire was used to collect information on duration of vegan diet, kind of diet before adopting the vegan diet, inclusion of eggs, milk and other dairy products in the diet. Furthermore the existence of inclusion and exclusion criteria was audited. The main questionnaire contained questions regarding anthropometric, socioeconomic and health oriented data [19].

All subjects were screened for health status by a general practitioner, who was a member of the GVS team, during time of blood collection. Standardization of screening was guaranteed by using a structured questionnaire that contained questions regarding major diseases (e.g. cancer, cardiovascular diseases, allergies), complications such as gastrointestinal problems as well as medication. Body weight was measured using a calibrated scale; body height, waist and hip circumference were surveyed via a tape measure. Body mass index (BMI) and waist-to-hip ratio (WHR) were computed using standard formulas. Pulse and blood pressure were recorded by a calibrated digital blood pressure meter.

A fasting venous blood sample was taken for the measurement of lipid parameters. Triacylglycerol concentrations were measured using an enzymatic colorimetric test (GPO-PAP, Boehringer, Germany). Total cholesterol was also assessed by an enzymatic colorimetric test (CHOD-PAP, Boehringer), while LDL concentrations were measured by precipitation with polyvinylsulfate (Boehringer) and HDL by precipitation with phosphotungstic acid (Boehringer). Kinetic nephelometry was used to measure Lp(a) (Beckman, Germany). An automated chemiluminescence system (ACS:180, Ciba Corning, Germany) was used to measure plasma cobalamin and red blood cell (RBC) folate concentrations [21–23]. Plasma homocysteine concentrations were measured using HPLC (Immunodiagnostic AG, Germany) [24]. Pyridoxine status was analyzed by measuring the erythrocyte aspartic acid aminotransferase (EAST) activity after stimulation (EPOS Analyzer 5060, Eppendorf/Hamburg, Germany) [25].

The following cut-off points were used to define abnormal (elevated or decreased) blood concentrations: TG >4.5 mmol/l, TC >5.2 mmol/l, LDL >3.5 mmol/l, HDL <0.9 mmol/l, TC/HDL >5, Lp(a) >30 mg/dl, homocysteine >10 μmol/l (>15 μmol/l), cobalamin <250 pmol/l (<150 pmol/l), folate 6.8 nmol/l, and alpha-EAST <1.85.

A statistical analysis program (SPSS 12.0, Chicago, Ill., USA) was used to analyze the data. The results are shown as mean ± SD and median plus 5th to 95th percentiles, respectively. The following two-tailed tests at the 5% level of significance were used to evaluate the study: In case of skewness, the Mann-Whitney U test was used in case of two independent samples (SV and MV). Given normal distribution, the independent sample t test was used. Normal distribution of data was checked visually and by using the Kolmogorov-Smirnov test. Dealing with nominal data, the χ^2 test was employed to evaluate statistically significant differences. Correlation analysis was done to reveal statistically significant associations between biochemical factors and dietary components. In case of skewness, the Spearman correlation coefficient was used, in case of normal distribution, Pearson's correlation coefficient was used. Predictors of homocysteine were evaluated by stepwise multiple linear regression. A general linear model revealed significant predictors of plasma cobalamin concentration.

Table 1. Anthropometric data and life-style factors of strict and moderate vegans (mean ± SD)

	Strict vegans (n = 98)	Moderate vegans (n = 56)	p
Gender distribution, % (females:males)	51.0:49.0	66.1:33.9	0.070[c]
Age, years	43.4 ± 15.4	45.7 ± 14.2	0.358[b]
BMI, kg/m^2	21.3 ± 2.73	21.3 ± 2.20	0.861[b]
WHR	0.82 ± 0.07	0.81 ± 0.08	0.244[b]
Systolic blood pressure, mm Hg	122 ± 19.6	117 ± 15.5	0.130[b]
Diastolic blood pressure, mm Hg	74.6 ± 11.1	75.9 ± 9.58	0.802[a]
Pulse rate, beats per min	70.5 ± 10.9	68.7 ± 8.83	0.316[b]
Physical activity			
Low	25.5%	17.9%	0.546[c]
Middle	48.0%	51.8%	
High	26.5%	30.4%	
Duration of vegan nutrition, years	7.70 ± 6.40	5.06 ± 4.03	0.058[a]
Smokers, %	3.06	3.57	0.864[c]

[a] Mann-Whitney U test; [b] t test for unpaired samples; [c] χ² test.

Table 2. Dietary intakes (total energy intake, relation of macronutrients, fatty acids, fiber and alcohol intake) of strict and moderate vegans (mean ± SD)

	Strict vegans (n = 98)	Moderate vegans (n = 56)	p
Energy intake, MJ/day	8.59 ± 2.97	7.60 ± 2.28	0.033[b]
Carbohydrates, % of energy	56.4 ± 7.74	58.6 ± 6.94	0.146[b]
Protein, % of energy	11.9 ± 2.11	11.0 ± 1.90	0.013[b]
Fat, % of energy	30.3 ± 8.22	28.8 ± 7.02	0.255[b]
Saturated fatty acids, % of energy	5.91 ± 1.66	6.16 ± 1.84	0.377[b]
Monounsaturated fatty acids (MUFA), % of energy	12.5 ± 5.50	12.3 ± 4.79	0.817[a]
Polyunsaturated fatty acids (PUFA), % of energy	9.06 ± 3.48	7.84 ± 2.78	0.026[b]
n–6 fatty acids, g/day	19.2 ± 10.4	14.4 ± 7.24	0.003[a]
n–3 fatty acids, g/day	1.98 ± 1.16	1.94 ± 1.13	0.791[a]
n–6:n–3	10.1:1	7.92:1	<0.001[b]
Alimentary cobalamin intake, μg/day (enriched/natural foods)	0.81 ± 1.74 (median: 0.29)	0.46 ± 0.81 (median: 0.23)	0.163[a]
Cholesterol, mg/day	18.0 ± 28.2	27.8 ± 23.7	<0.001[a]
Fiber, g/day	58.6 ± 22.2	53.5 ± 14.9	0.125[b]
Alcohol consumption, g/day	0.66 ± 3.15	0.97 ± 3.13	0.084[a]

[a] Mann-Whitney U test; [b] t test for unpaired samples.

Results

Altogether 154 subjects (98 SV and 56 MV) participated in all parts of the study (pre- and main questionnaire, two 9-day food-frequency questionnaires, and blood sampling) and fulfilled all the study criteria and did not fulfil any of the exclusion criteria. Table 1 shows that strict and moderate vegans did not differ in anthropometric characteristics and life-style factors. The proportion of females was higher in the moderate vegan subgroup than in the strict vegan subgroup, but this difference missed statistical significance. As indicated in table 2, the subgroups differed significantly regarding energy intake, protein intake, energy derived from poly unsaturated fat-

Table 3. Serum lipid profile of strict and moderate vegans (median, 5th to 95th percentile)

	Strict vegans (n = 98)	Moderate vegans (n = 56)	p
Triacylglycerol, mmol/l	0.81 (0.40/1.67)	0.81 (0.46/2.67)	0.724[a]
Total cholesterol, mmol/l	4.31 (2.82/6.07)	4.44 (3.20/7.21)	0.044[b]
LDL, mmol/l	2.41 (1.27/3.97)	2.53 (1.48/5.14)	0.108[b]
HDL, mmol/l	1.31 (0.81/1.86)	1.40 (0.86/2.05)	0.070[b]
Total cholesterol/HDL	3.27 (2.14/5.80)	3.38 (2.0/5.19)	0.759[a]
Lipoprotein(a), mg/dl	9.40 (2.00/114)	6.73 (2.00/92.0)	0.110[a]

[a] Mann-Whitney U test; [b] t test for unpaired samples.

Table 4. Plasma homocysteine and related vitamin status (median, 5th to 95th percentile)

	Strict vegans (n = 98)	Moderate vegans (n = 56)	p
Plasma homocysteine, µmol/l	13.3 (5.97/82.0)	11.1 (3.60/25.7)	0.004[a]
% with homocysteine >10 µmol/l	71.1	57.1	
Hcys <10 µmol/l + duration of vegan diet			
<5 years	65.5	50	
5–<10 years	77.3	66.7	
>10 years	80	100	
Serum cobalamin, pmol/l	130 (72.1/294)	187 (93.6/748)	<0.001[a]
% with cobalamin <250 pmol/l	86.5	69.1	
Cob. <250 pmol/l + duration of vegan diet			
<5 years	85.2	73.7	
5–<10 years	77.3	57.1	
>10 years	100	66.7	
RBC folate, mmol/l	33.0 (18.1/46.5)	35.8 (17.8/45.3)	0.644[b]
Alpha-EAST	1.60 (1.30/2.00)	1.60 (1.26/2.00)	0.375[a]

[a] Mann-Whitney U test; [b] t test for unpaired samples.

ty acids (PUFA), intake of n–6 fatty acids, relation of n–6 to n–3 fatty acids, and cholesterol intake: energy, protein, n–6 fatty acid intake and energy from PUFA were significantly higher in the SV study population, while cholesterol intake was significantly higher in the MV study population. As shown in table 3, median triacylglycerol, total cholesterol, LDL, HDL, and Lp(a) serum concentrations as well as the ratio of TC to HDL did not reach dimensions that are associated with an increased CHD risk (TG >4.5 mmol/l, TC >5.2 mmol/l, LDL >3.5 mmol/l, HDL <0.9 mmol/l, TC/HDL >5, Lp(a) >30 mg/dl) [26]. Only total cholesterol differed statistically significantly between the subgroups, a higher median concentration was found in the MV subgroup. In the total study population the ratio of total cholesterol to HDL was 3.3 (2.20/5.47). Of the SV 9.3% and 5.4% of the MV showed a TC/HDL ratio >5. Plasma homocysteine concentrations and status of related vitamins are shown in table 4. A general linear model (p = 0.002; R^2 = 0.119) revealed dietary subgroup (beta = 0.043, p = 0.012), gender (beta = 0.027, p = 0.049) as significant predictors of plasma cobalamin concentration, while duration of vegan diet (beta = 0.011, p = 0.207) and cobalamin intake (beta = 0.008, p = 0.285) increased the fraction of explained variance marginally. In general, status of folate and pyridoxine was sufficient, while 58.3% of SV and 34.5% of MV (p = 0.005) were cobalamin deficient (i.e. cobalamin <150 pmol/l). Using a higher cut-off point of 250 pmol/l 86.5% of SV and 69.1% of MV (p = 0.010), respectively, were considered as cobalamin deficient. When the dietary subgroups were differentiated according to duration of vegan diet (<5 years, 5 to <10 years, >10 years) no clear association between the prevalence of cobalamin deficiency and the duration of vegan diet was seen: Persons in the middle time category were less affected by cobalamin deficiency than in the other catego-

Table 5. Multiple regression of homocysteine (log)

	Standardized regression coefficients					
	total study population (n = 154)		strict vegans (n = 98)		moderate vegans (n = 56)	
	beta	p	beta	p	beta	p
Duration of vegan nutrition, years	0.428	<0.001	0.447	<0.001	0.301	0.004
Serum cobalamin, pmol/l	−0.451	<0.001	−0.386	<0.001	−0.600	<0.001
Adjusted R²	0.443		0.396		0.470	

No significant relationship to gender, age, RBC folate concentrations and alpha-EAST activity coefficient (pyridoxine status), dietary folate, pyridoxine and cobalamin.

ries. However, in all time categories more SV than MV showed cobalamin concentrations <250 pmol/l. Elevated homocysteine concentrations (i.e. homocysteine >10 μmol/l) were present in 71.1% of SV and 57.1% of MV. The combination of elevated homocysteine (>10 μmol/l) and low cobalamin concentration (<250 pmol/l) was found in 61.6% of the study population (SV: 67.7%, MV: 50.9%; p = 0.041). When the dietary subgroups were differentiated according to duration of vegan diet (<5 years, 5 to <10 years, ≥10 years) prevalence of elevated homocysteine concentrations increased with proceeding duration of vegan diet.

To analyze the relationship between homocysteine and influencing variables a stepwise multiple linear regression was carried out. In both, strict and moderate vegans, time of adhering to the vegan diet and cobalamin concentrations were predictors of homocysteine concentrations (table 5).

Discussion

Known risk factors such as hypertension, elevated cholesterol, smoking, and/or elevated plasma triacylglycerol contribute to 50% of CHD. Therefore, there must be other factors that are associated with the development of CHD [27]. Two of these other factors may be elevated plasma homocysteine and Lp(a) concentrations, which have been shown to be associated with an increased risk of cardiovascular diseases [14, 28]. Epidemiological data show that vegetarians and vegans are at relatively low risk for CVD [17, 18] when considering conventional risk factors (e.g. total cholesterol, LDL, BMI, smoking, and alcohol consumption), but knowledge about Lp(a) and homocysteine levels in vegans is still limited. For this reason

the present study aimed at evaluating conventional CVD risk factors, homocysteine and Lp(a) concentrations in a vegan study population, which was divided into strict and moderate vegans. Focusing on life-style factors such as smoking, alcohol consumption, and physical activity it is obvious that the GVS study population was extremely health conscious. Only 3% of the study population smoked and nearly 40% of the study population consumed no alcohol at all. This may partly be due to the fact that overall 35% of the study population were Seventh-day Adventists, who are especially health conscious [29,30]. Our findings bear analogy to findings from other studies that report a comparatively high health consciousness in cohorts with vegetarian life-styles [31–34].

Low mean BMI and WHR reflect low mean energy intake in the study population. The distribution of main nutrients to total energy intake meets the current recommendations of nutrition societies [35]. Carbohydrates were the main nutrients with an energy contribution of nearly 60%, whereas fats contributed to energy supply with nearly 30% of total energy intake. In regard to the fatty acid composition, the dietary pattern of the GVS study population fulfilled current recommendations of the NCEP (National Cholesterol Education Programme) [36] and the International Task Force for the Prevention of Coronary Heart Disease [26]. But relation of n–6:n–3 fatty acid intake was lower than the recommended relation for vegetarian and vegan populations of 2:1 to 4:1 [37]. Mean fibre intake was nearly 60 g/day and was nearly twice the current recommendation to ingest 30 g/day [35]. The high fibre intake is the consequence of the high fruit and vegetable intake of the study population (1,458 ± 673 g/day). Alimentary cobalamin intake was higher in strict vegans than in moderate vegans due to the higher use of enriched foods in the SV subgroup. There might be an overestimation of the in-

gested amount of vitamin B_{12} in the SV subgroup due to varying cobalamin contents of enriched foods and due to the insecurity of the bioactivity of the cobalamin compounds that were used for enrichment.

The present study shows that vegans have a low risk lipid profile. This is especially obvious for LDL, triacylglycerol and the TC/HDL ratio. Only 7.2% of the total study population showed a TC/HDL ratio >5, which is considered as a risk factor for CHD [26]. However, HDL was low while Lp(a) and homocysteine are elevated in our study population. Our findings confirm data from previous studies with vegetarian [38–40] and vegan cohorts [4, 39, 40] which show that a plant-based diet is related to a favourable lipid profile on the one hand, and that homocysteine is more likely to be elevated in strict vegetarians (vegans) on the other hand. Elevated homocysteine concentrations may result from genetic defects [41], from deficiencies of cobalamin, folate, and/or pyridoxine. Thus, the adequate intake of these vitamins can optimize the homocysteine concentration [27]. In omnivores hyperhomocysteinemia is mostly due to a low intake of folate or pyridoxine. In persons with high folic acid intakes [42] as well as in vegetarians and especially in vegans hyperhomocysteinemia is rather the consequence of cobalamin deficiency [39,43]. We also did not find correlations for RBC folate ($r_s = 0.033$; p = 0.689) and pyridoxine ($r_s = -0.08$; p = 0.342) status with homocysteine, but for cobalamin and homocysteine ($r_s = -0.684$; p < 0.001). Gerhard and Duell [9] recommend concentrations of <10 µmol/l in CHD prevention. Homocysteine concentrations above this cut off were prevalent in 66% of the study population. Most of these participants showed decreased cobalamin concentrations (<150 pmol/l, 67%; <250 pmol/l, 93%), while folate and pyridoxine status were sufficient. The lack of a significant influence of cobalamin intake on serum concentrations in our study population may be due to the low variability of cobalamin intake and/or the alleged higher alimentary intake in the SV subgroup, which ingested cobalamin in form of enriched foods. Intervention studies show that an additional cobalamin intake can sufficiently increase low serum concentrations and decrease elevated homocysteine concentrations [44]. Multiple linear regression analysis showed that cobalamin status and duration of adhering to the vegan diet were predictive for the homocysteine concentrations in our collective. In other studies on vegans more than half of the participants showed homocysteine concentrations >15 µmol/l [7, 39, 43], while 35% of our study population showed homocysteine concentrations above this value. The prevalence of homocysteine concentrations >15 µmol/l ascended with proceeding duration of vegan diet (<5 years, 25.8%; 5 to <10 years, 37.8%; ≥10 years, 69.6%; p < 0.001). The high prevalence of elevated homocysteine in vegans reported here and elsewhere may provide one mechanistic explanation for the observation that CHD death rates are higher in vegans than in lacto-ovo-vegetarians [18]. In patients with CHD or in patients at significant risk for CHD, Lp(a) should be measured. Levels >10 mg/dl should be treated with either high therapeutic doses of niacin or estrogen [10]. In the present study Lp(a) concentrations varied greatly. Nearly 46% of the participants had Lp(a) concentrations above 10 mg/dl. In general an Lp(a) concentration of more than 30 mg/dl is accepted as a risk threshold for developing cardiovascular disease in apparently healthy persons [45]. A quarter of our study population showed these elevated Lp(a) concentrations. Li et al. [46] compared omnivore and vegetarian women regarding their lipid profile and Lp(a) status. In their study cohort, Lp(a) concentrations were higher in omnivore women than in vegetarian. A significant negative correlation was found between Lp(a) concentrations and carbohydrate intake. In our study, we were not able to confirm the latter finding. This may partly be due to the wide variation in Lp(a) concentrations in the GVS study population.

A limitation of this study is that there was no control group. The results were compared between strict vegans and moderate vegans that differed only slightly but an in important dietary behavior: The inclusion of small amounts of foods of animal origin. Due to the lack of an omnivore control group it might be possible that the observed effects that were interpreted as a dietary subgroup allocation effect might be overestimated.

Conclusion

Although total and LDL cholesterol concentrations were favourable, low HDL cholesterol, elevated homocysteine, and lipoprotein(a) concentrations were unfavourable. Overall, these results confirm the notion that a vegan diet is deficient in vitamin B_{12}, which may have an unfavorable effect on CHD risk.

Acknowledgement

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