Acute Effect of Drinking Red and White Wines on Circulating Levels of Inflammation-Sensitive Molecules in Men With Coronary Artery Disease

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There is evidence that moderate consumption of red wine with its high content of polyphenolic antioxidants may be more protective than white wine against development of coronary artery disease (CAD). The aim of this study was to compare the acute effects of ingestion of red wine and white wine on markers of inflammation in men with CAD. Thirteen men with angiographically-proven CAD were studied in a cross-over trial. The men consumed 4 mL/kg (2 to 3 glasses) red wine and white wine in random order during a light meal and with at least a week between interventions. Later, the men also consumed an isoenergetic nonalcoholic beverage (control) in the same study protocol. Venous blood was taken at baseline, 1 hour, and 6 hours after the drinks. Plasma interleukin-6 (IL-6), vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), blood alcohol, plasma lipids, and plasma polyphenols were measured. Mean ± SD blood alcohol was 6.5 ± 2.2 mmol/L and 6.9 ± 1.1 mmol/L at 1 hour and returned to baseline at 6 hours after intake of red wine and white wine, respectively. Plasma IL-6 concentration increased significantly ($P = .01$) during 6 hours after ingestion of red wine (56%) and white wine (63%). The increase in plasma IL-6 concentration after ingestion of wine was significantly higher ($P = .045$) compared with the corresponding increase (11%) following intake of the nonalcoholic beverage. Plasma IL-6 levels at 6 hours ($r = .631$, $P = .02$) were correlated significantly with plasma alcohol levels at 1 hour after ingestion of red wine. These data suggest that moderate wine intake may acutely increase plasma levels of IL-6 in men with CAD. It is possible that this increase in plasma IL-6 is a response to alcohol-induced oxidative stress in the liver.

EPIDEMIOLOGIC STUDIES indicate that regular consumption of moderate amounts of alcoholic beverages (1 to 2 drinks per day) is associated with lower risk of coronary heart disease (CHD).[1-5] There is evidence that red wine provides extra cardioprotection compared with other alcoholic beverages.[4-6] High content of polyphenolic antioxidants in red wine is thought to decrease the risk of CHD by attenuating the oxidation of low-density lipoprotein (LDL),[7] decreasing inflammatory activity,[8] and improving impaired endothelial function.[9,10] Phenolic antioxidants from red wine inhibit the upregulation of nuclear factor-κB (NF-κB), which is a redox-sensitive nuclear transcription factor with a key role in immune and inflammatory response, in isolated monocytes.[8] Also, ingestion of red wine attenuates activation of monocyte NF-κB in healthy subjects during postprandial lipemia after a fatty meal.[8] NF-κB acts on genes that regulate synthesis of proinflammatory cytokines, chemokines, and cell adhesion molecules.[11] Resveratrol, a phytoalexin present in wine, inhibits the expression of vascular cell adhesion molecule-1 (VCAM-1) on cultured endothelial cells.[12]

Cell adhesion molecules mediate the binding of circulating monocytes to the vascular endothelium. This is a crucial step in the response of tissues to inflammation and in the development of the atherosclerotic lesion.[13] Interleukin-6 (IL-6) is classified as both a proinflammatory and anti-inflammatory cytokine and is postulated to play a role in atherogenesis.[14] Plasma concentrations of IL-6[15] and soluble cell adhesion molecules[16] are elevated in patients with coronary artery disease (CAD) compared with matched controls. Whether or not ingestion of red wine decreases plasma concentrations of IL-6 and cell adhesion molecules is unclear. Few studies have examined the acute effect of red wine and white wine intake on circulating levels of proinflammatory cytokines and cell adhesion molecules in men with CAD. Recently, we have reported a 2- to 3-fold increase in endothelium-dependent vasodilation indicating improved endothelial function at 6 hours after ingestion of red and white wines in men with angiographically proven CAD.[17] To define further the acute effect of wine on endothelial function and inflammation in men with CAD, we have measured postprandial plasma concentrations of IL-6, VCAM-1, and intercellular adhesion molecule-1 (ICAM-1) after ingestion of moderate amounts of red wine and white wine with a light meal.

SUBJECTS AND METHODS

Subjects

Men aged 48 to 70 years with angiographic evidence of CAD were eligible to participate in the study. Men who had experienced an acute coronary event within the preceding 60 days, had significant renal or hepatic disease, uncontrolled hypertension, diabetes mellitus, a recent history of smoking cigarettes, a history of alcohol dependence or abuse, or were receiving oral anticoagulant therapy were excluded. The self-reported drinking habits of the subjects were recorded. Fourteen men who met these criteria were recruited into the study. One subject was excluded from the present study due to insufficient stored plasma for measurement of cytokines at all time points. All subjects gave written and informed consent, and the study was approved by the Otago Ethics Committee.

Study Protocol

The present study was performed on blood samples collected during a study designed to test the effect of red wine and white wine on endothelium-dependent flow-mediated vasodilation in men with CAD.[17] Subjects were instructed to refrain from drinking alcohol for 1 week before each study visit. They were also instructed to maintain

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their usual diet and to continue taking their medication in the period between visits and to refrain from taking medications on the morning of each visit. On study days, the men were instructed to consume a light breakfast consisting of 2 slices of toast with jam at home before reporting to the study center at 9 AM. Tea, coffee, and fruit juices were not permitted. Anthropometric data were recorded, and blood pressure was measured 3 times and the mean pressures were calculated. Subjects were randomized to receive red wine (Stoneleigh Marlborough Pinot Noir, New Zealand, 1998) or white wine (Jackson Estate Marlborough Sauvignon Blanc, New Zealand, 1998) followed by the alternate wine with an interval of at least a week between each intervention. The men received the wines at a dose of 4 mL/kg body weight (2 to 3 glasses) that is equivalent to an intake of 0.52 g alcohol/kg body weight for both wines. Test beverages were consumed with a light meal that was low in antioxidants. This meal was designed to minimize the influence of nutrient and antioxidant intake on study variables while complying with the dictum that alcoholic beverages should be consumed with food. The meal consisted of a small bread roll (58 g) filled with 5 g margarine, 2 leaves of lettuce, half a tomato sliced, a slice of low-fat cheese (25 g), a low-fat yogurt (200 g), and a banana (total energy, 2,222 kJ (513 kcal); carbohydrate, 62% energy; protein, 18% energy; fat, 20% energy). The meal was consumed within 20 minutes at 10:30 AM. During the following 6-hour test period, subjects did not consume any food and were permitted only bottled water to drink. Three months after the wine study, the subjects ingested an isoenergetic, nonalcoholic beverage with the light meal in an identical protocol. The nonalcoholic beverage was a raspberry cordial (Schweppes, Auckland, New Zealand). Venous blood was taken at baseline and at 1 hour and 6 hours after consumption of each test beverage. Plasma levels of IL-6, cell adhesion molecules, total phenolic compounds, lipids, high-density lipoprotein (HDL) cholesterol, glucose, and alcohol were measured.

Laboratory Methods

Aliquots of plasma were kept at −80°C. Plasma concentrations of IL-6, soluble VCAM-1, and soluble ICAM-1 were measured in duplicate by enzyme-linked immunosorbent assay (ELISA) using commercial kits (R&D Systems, Minneapolis, MN). All samples from an individual after wine intake were measured in the same run. Plasma concentration of phenolic compounds was measured by a colorimetric method using the Folin-Ciocalteu Phenol reagent[18] and a gallic acid standard. Phenolic compounds in wine were measured by a similar method.[19] Plasma lipids were measured by automated methods using commercial kits (Roche, Boehringer Mannheim, Germany). HDL cholesterol was measured in the supernatant after precipitation of apolipoprotein B-containing lipoproteins with dextran sulphate and magnesium chloride.[20] Plasma glucose and alcohol concentrations were determined by routine methods in the laboratories of HealthLab Otago (Dunedin, New Zealand). The method used for measurement of plasma alcohol concentration is not designed to measure the low levels of endogenous ethanol.

Statistical Analysis

The SPSS 10 statistical package (SPSS, Chicago, IL) was used to analyze the data. Repeated measures analysis of variance (ANOVA) was used to test data for effects of the type of wine, time after ingestion of the wine plus meal, and the interaction between these factors. Order of red wine and white wine intake was taken into account in these analyses. If a significant change with time was detected, within-subjects contrasts were used to compare 1-hour and 6-hour levels with baseline. Repeated measures ANOVA was also used for the secondary analysis of the combined data obtained from the wine and nonalcoholic beverages studies. Order of the beverage intake was not included in this analysis because subjects were not randomized to the nonalcoholic beverage. Tables include statistical data from both the wine and all beverages analyses. Values of IL-6 and cell adhesion molecules were log-transformed before analysis. Paired *t* tests were used to compare baseline values before ingestion of the wines. Pearson's product-moment correlation coefficients were used to test for relationships between variables. Two-tailed tests of significance were used, and a *P* value of less than .05 was considered to be statistically significant.

Table 1. Characteristics of the Men With CAD (n = 13)

Age (yr)	59 ± 7
Weight (kg)	86 ± 13
BMI (kg/m^2)	27.9 ± 4.1
Systolic blood pressure (mm Hg)	135 ± 11
Diastolic blood pressure (mm Hg)	82 ± 7
Aspirin therapy (%)	100
ACE inhibitor therapy (%)	54
Beta-blocking therapy (%)	85
Statin therapy (%)	85
Reported alcohol intake	
Occasionally/never (n)	7
<1 drink/day (n)	1
1-2 drinks/day (n)	4
> 2 drinks/day (n)	1

NOTE. Values are mean ± SD or percent.

Abbreviations: BMI, body mass index; ACE, angiotensin converting enzyme.

RESULTS

The characteristics of the subjects are shown in Table 1. All men were receiving aspirin therapy, and most were also receiving treatment with statins and β-blocking drugs. Approximately half of the men were taking angiotensin-converting enzyme (ACE) inhibitor drugs. Nearly all the men were light to moderate consumers of alcohol. The mean (± SD) volume of wine and alcohol consumed during the study were 340 ± 52 mL and 44.2 ± 6.8 g, respectively. The concentrations of phenolic substances in the red wine and the white wine were 1,170 mg/L and 210 mg/L, respectively. The raspberry cordial contained 0.2 mg/L phenolic compounds. These values are expressed as gallic acid equivalents.

Table 2 shows plasma alcohol concentration, blood pressure, and heart rate in the men during the postprandial period after ingestion of red and white wines and a nonalcoholic beverage with a light meal. At baseline, exogenous alcohol was not detectable in plasma from the men. At 1 hour after wine intake, plasma alcohol concentration increased to detectable levels that were not significantly different between red wine and white wine. At 6 hours, exogenous alcohol was again undetectable in plasma. Systolic and diastolic blood pressure decreased significantly, and heart rate increased significantly early after ingestion of the alcoholic beverages. These changes were not significantly different between red wine and white wine intake and were not significantly different from the corresponding changes after intake of the nonalcoholic beverage (control).

Table 3 summarizes plasma lipids, lipoproteins, polyphenol, and glucose concentrations after intake of red and white wines and a nonalcoholic beverage with a light meal. Plasma triglyceride concentration increased significantly, and plasma HDL cholesterol and plasma glucose decreased significantly during 6 hours after intake of the wines. These changes were not sig-

Table 2. Plasma Alcohol Concentration, BP, and Heart Rate After Ingestion of Red and White Wines and a NAB With a Light Meal

	Time (h)	Red Wine	White Wine	NAB	P* Wines	*P** All Beverages
Alcohol (mmol/L)	0	e	e	e		
	1	6.5 ± 2.2	6.9 ± 1.1	e		
	6	e	e	e		
Systolic BP (mm Hg)	0	135 ± 11	136 ± 14	135 ± 15		
	1	122 ± 8†	123 ± 11†	129 ± 11†	0.47	.21
	6	137 ± 13	134 ± 15	137 ± 14		
Diastolic BP (mm Hg)	0	82 ± 7	82 ± 7	80 ± 7		
	1	74 ± 6†	73 ± 8†	73 ± 6†	0.92	.99
	6	83 ± 9	83 ± 11	82 ± 8		
Heart rate (beats/min)	0	55 ± 11	56 ± 11	56 ± 10		
	1	60 ± 12†	60 ± 12†	58 ± 10†	0.82	.15
	6	54 ± 11	55 ± 9	55 ± 9		

NOTE. Values are mean ± SD.

Abbreviations: e, not above endogenous concentrations of ethanol; BP, blood pressure; NAB, nonalcoholic beverage.

*Significance of wine (beverage) × time interactions from repeated measures ANOVA.

†$P \leq .001$ compared with baseline using within subjects contrasts of time effect in repeated measures ANOVA.

nificantly different between red wine and white wine intake. Plasma glucose was significantly ($P = .02$) higher at baseline before ingestion of red wine and remained significantly higher ($P = .04$) compared with levels during the white wine arm of the study. Plasma polyphenol concentrations did not change significantly during the study. The increase in plasma triglyceride concentration after ingestion of the nonalcoholic beverage was significantly less ($P < .001$) compared with the corresponding increases after intake of red and white wines. The decrease in plasma HDL cholesterol was not significantly different following ingestion of the nonalcoholic beverage and the wines. Plasma HDL cholesterol was significantly higher ($P = .002$) at all times during the nonalcoholic beverage phase of the study. The change in plasma glucose concentration after the nonalcoholic drink was significantly different ($P = .01$) compared with the decrease after intake of the wines. This was due to significantly different ($P = .01$, beverage × time within subject contrast) changes in plasma glucose concentration during the first hour after drinking the beverages.

Plasma concentrations of IL-6 and cell adhesion molecules during the study are shown in Table 4. Plasma IL-6 concentration increased significantly after intake of both red and white wines, and concentrations at 6 hours were significantly higher ($P = .01$) compared with baseline values. Plasma levels of cell adhesion molecules did not change significantly during the study. The order in which the wines were consumed did not significantly influence these findings. Plasma IL-6 concentration also increased significantly ($P = .02$) at 6 hours after

Table 3. Plasma Lipids, Lipoproteins, Polyphenols, and Glucose Concentrations in Men With CAD After Ingestion of Red and White Wines and a NAB With a Light Meal

	Time (h)	Red Wine	White Wine	NAB	*P** Wines	*P** All Beverages
TG (mmol/L)	0	1.50 ± 0.53	1.45 ± 0.54	1.63 ± 0.91		
	1	1.75 ± 0.59‡	1.61 ± 0.56‡	1.76 ± 0.91‡	.48	<.001
	6	2.40 ± 0.69‡	2.26 ± 0.69‡	1.96 ± 1.03‡		
TC (mmol/L)	0	4.19 ± 0.64	4.10 ± 0.63	3.94 ± 0.64		
	1	4.20 ± 0.54	4.08 ± 0.62	3.77 ± 0.70	.65	.25
	6	4.31 ± 0.62	4.16 ± 0.70	3.96 ± 0.76		
HDL-C (mmol/L)	0	1.10 ± 0.17	1.08 ± 0.15	1.20 ± 0.24§		
	1	1.07 ± 0.18‡	1.06 ± 0.17‡	1.19 ± 0.25§	.91	.83
	6	1.03 ± 0.17‡	1.02 ± 0.16‡	1.15 ± 0.23‡§		
PP (mmol/L)	0	12.48 ± 1.03	12.41 ± 0.98	12.54 ± 0.47		
	1	12.27 ± 0.63	12.22 ± 0.61	12.54 ± 0.56	.70	.63
	6	12.49 ± 0.68	12.67 ± 0.94	12.54 ± 0.59		
Glucose (mmol/L)	0	6.0 ± 1.1‖	5.4 ± 0.9	5.2 ± 0.8		
	1	5.4 ± 1.0‖	5.1 ± 1.0	6.0 ± 1.2	.25	.01
	6	4.9 ± 0.7†‖	4.8 ± 0.4†	4.6 ± 0.3†		

NOTE. Values are mean ± SD (n = 13).

Abbreviations: TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; PP, polyphenols.

*Significance of wine (beverage) × time interactions in repeated measures ANOVA.

†$P < .05$, ‡$P < .01$, compared with baseline using within subjects contrasts of time effect.

§$P = .002$ compared with wines, ‖$P = .04$ compared with white wine (ANOVA).

Table 4. Plasma IL-6, Cell Adhesion Molecule Concentrations in Men With CAD After Ingestion of Red and White Wines and a NAB With a Light Meal

	Time (h)	Red Wine	White Wine	NAB	*P** Wines	*P** All Beverages
IL-6 (ng/L)	0	1.64 (0.94, 2.39)	1.30 (0.96, 2.14)	1.76 (1.20, 3.05)		
	1	1.76 (1.28, 2.38)	1.26 (1.00, 2.02)	1.76 (0.93, 2.31)	.06	.045
	6	2.56 (1.58, 3.05)‡	2.12 (1.34, 2.91)‡	1.96 (1.38, 2.73)†		
ICAM-1 (μg/L)	0	237 (187, 267)	240 (200, 261)	260 (219, 294)		
	1	234 (186, 270)	208 (189, 266)	243 (210, 301)	.77	.77
	6	240 (198, 259)	234 (191, 263)	252 (207, 293)		
VCAM-1 (μg/L)	0	580 (481, 698)	583 (486, 605)	548 (476, 706)		
	1	572 (474, 663)	561 (505, 592)	613 (469, 750)	.94	.64
	6	547 (487, 622)	537 (450, 598)	524 (441, 678)		

NOTE. Values are median (interquartile range) (n = 13).

Abbreviations: IL-6 interleukin-6; CRP, C-reactive protein; ICAM-1, soluble intercellular adhesion molecule-1; VCAM-1, soluble vascular cell adhesion molecule-1. Data were log-transformed before analysis by repeated measures ANOVA.

*Significance of wine (beverage) × time interactions; †$P = .02$; ‡$P = .01$ compared with baseline using within subject contrasts.

ingestion of the nonalcoholic beverage, and this increase was significantly smaller ($P = .045$) than the corresponding increases after wine intake.

Plasma IL-6 concentration at 6 hours was correlated significantly ($r = .631$, $P = .02$) with the plasma alcohol concentration at 1 hour after drinking red wine. The corresponding correlation for white wine did not achieve statistical significance ($r = .223$).

DISCUSSION

The present data indicate that ingestion of 2 to 3 glasses of red wine or white wine with a light meal both acutely increase plasma IL-6 concentration at approximately 6 hours, but do not appreciably alter plasma concentrations of soluble cell adhesion molecules in men with CAD. Thus, the higher content of phenolic antioxidants in red wine did not appear to acutely influence levels of inflammation-sensitive molecules in these men.

It is possible that increased levels of alcohol may be partly responsible for the acute increase in plasma IL-6 after drinking wine in men with CAD. The 1-hour concentration of alcohol in plasma was associated with the increase in plasma IL-6 during 6 hours following ingestion of red wine with the light meal. On the other hand, plasma alcohol levels at 1 hour after drinking white wine were similar to the corresponding levels after red wine intake, but did not predict 6-hour plasma IL-6 concentrations. The 1-hour plasma alcohol concentration may not reliably reflect exposure of the body to the effects of alcohol during the 6-hour postingestion period. Animal studies suggest that alcohol intake may increase the secretion of IL-6 in a process that may be mediated by increased oxidative stress. An increase in plasma IL-6 and hepatic levels of reactive oxygen species in mice given a single dose of alcohol has been reported previously.[21] Acute alcohol ingestion increases oxidative stress through its microsomal metabolism by cytochrome P4502E1 and initiates free radical reactions in the liver.[22] It is possible that an acute increase in plasma IL-6 following ingestion of wine with a light meal may be a protective response to alcohol-induced increase in hepatic oxidative stress. In vitro, IL-6 inhibits hepatocyte generation of reactive oxygen species stimulated by ethanol and tumor necrosis factor-α (TNF-α) and protects the cells from apoptosis.[23] The liver can synthesize IL-6[24,25] and is a potential source of the acute increase in plasma IL-6 following ingestion of wine in the present study.

The increase in plasma IL-6 following ingestion of wine did not appear to be due to increased systemic inflammation. Plasma concentrations of VCAM-1 and ICAM-1 were unchanged and flow-mediated dilation of the brachial artery was increased 2- to 3-fold at 6 hours following ingestion of red and white wines.[17] Upregulation of cell adhesion molecule expression would be expected to accompany a significant level of systemic inflammation. Also, improved endothelial function is not in keeping with increased systemic inflammation. A previous study has reported that acute, mild systemic inflammation as a result of vaccine administration acutely impairs flow-mediated vasodilation in healthy subjects.[26] Plasma IL-6 levels increased, but may not be responsible for the impaired endothelial function following vaccination.[26] IL-6 does not decrease mRNA encoding endothelial nitric oxide synthetase in human veins.[27] Whether elevated levels of triglyceride-rich lipoproteins increase plasma IL-6 concentration at 6 hours after wine intake is uncertain. Previous studies have reported that very–low-density lipoprotein (VLDL) has proinflammatory activity[8,28] and that alcohol intake increases postprandial levels of VLDL.[8]

Plasma IL-6 is subject to diurnal variation, and levels increase slowly during the day to reach a maximum at night.[29] Thus, diurnal variation may contribute to the relatively small (11%) increase in plasma IL-6 following the intake of the nonalcoholic drink plus the light meal. Endothelium-dependent vasodilation was unchanged[17] suggesting that endothelial metabolism was not appreciably perturbed in the hours after consumption of the nonalcoholic drink.

The absence of a differential effect of red wine compared with white wine intake on potentially oxidant-sensitive variables in the present study may be due to the finding that plasma levels of phenolic compounds did not change appreciably after ingestion of either wine. This failure to detect an increase in phenolic compounds may be due to the 1-hour and 6-hour sampling times. A previous study using a similar method for

measuring phenols has reported a peak in plasma phenolic compounds at 30 minutes and returning to baseline at approximately 1 hour after red wine intake.[18] Regular consumption of wine may be necessary to increase plasma phenolic antioxidants to levels that might influence inflammatory activity. On the other hand, studies have reported an acute decrease in a mediator of inflammation (NF-κB)[8] and an increase in antioxidant capacity[30] after ingestion of red wine that was attributed to increased intake of phenolic compounds. Another study has reported an increase in total plasma radical trapping in diabetic patients within 3 hours after ingestion of red wine.[30] We cannot exclude the possibility that the red wines used in these studies may have contained higher levels of certain bioactive polyphenols compared with the red wine that was used in the present study.

In healthy subjects, ingestion of red wine with the daily diet decreases postprandial peaks in blood glucose.[31] It is possible that this effect of wine may contribute to the failure of plasma glucose levels to increase at 1 hour following the intake of wine with a light meal in the present study. When a nonalcoholic, isoenergetic cordial was consumed with the light meal, plasma glucose concentration was increased 1 hour later. The higher baseline levels of plasma glucose in men immediately prior to intake of red wine may be a chance finding because they were randomized to the order of red and white wine intake.

The 2 to 3 glasses of wine consumed by men in the present study represents a moderate daily intake of alcohol and is not substantially more than the 1 to 2 alcoholic drinks per day that is reported to protect against CHD in epidemiologic studies. Also, drinking 2 to 3 glasses of wine with a light meal did not appear to result in circulating levels of alcohol that would be expected to appreciably impair motor skills. The plasma alcohol concentration attained 1 hour after the wine plus light meal was below the legal limit (17.4 mmol/L, 80 mg/dL) for driving a motor vehicle in New Zealand.

This study has limitations. The sample size was relatively small. Thus, care should be exercised in extrapolating the findings to larger populations of men with CAD. The men were not blinded to the type of drink they ingested. However, the acute nature of the studies provided little opportunity for this factor to bias data. The 1-week period immediately prior to each study visit during which the men abstained from alcoholic beverages may have been insufficient to reverse any effect of their regular alcohol consumption on our findings. On the other hand, the majority of the men did not drink alcohol daily and had relatively low intake. The men were not randomized to receive the nonalcoholic drink, and this arm of the study was conducted after the wine studies. Consequently, these data may be potentially influenced by changes in lifestyle and other factors in the intervening period. It is possible that a decrease in plasma volume as a result of the diuretic effect of alcohol may contribute to the increase in plasma IL-6 concentration with wine intake. However, the magnitude of such an increase is probably small (4%) compared with the magnitude (56% and 63%) of the increase in plasma IL-6 following ingestion of red and white wines. A previous study has reported a 4% increase in venous hematocrit in subjects at 3 hours after a single moderate dose of alcohol.[32]

An increase in plasma IL-6 could potentially have an adverse effect on atherosclerotic lesions in subjects with CAD. IL-6 is localized in human coronary atherosclerotic lesions[33] and stimulates the activity of matrix-degrading proteins[34,35] that may promote plaque instability. On the other hand, it is uncertain whether an acute (or prolonged) increase in plasma IL-6 is capable of stimulating metalloproteinase activity in atherosclerotic lesions in men with CAD. Also, the substantial increase in endothelium-dependent vasodilation in the present study[17] suggests that arterial metabolism may be acutely improved by ingestion of wine, despite an increase in plasma IL-6 levels. An acute increase in plasma IL-6 concentration does not necessarily have an adverse effect on human health. IL-6 has anti-inflammatory activity that may limit the production of the proinflammatory cytokines IL-1 and TNF-α.[36,37] Physical exercise acutely increases plasma levels of IL-6,[38] but has an overall beneficial effect on health.

In conclusion, the present data indicate that ingestion of moderate amounts of both red and white wines acutely increase plasma IL-6 concentration in men with CAD to levels comparable to those previously documented during mild inflammation.[26] We postulate that the acute increase in plasma IL-6 after ingestion of wine may be a protective response to alcohol-induced oxidative stress in the liver. This increase in plasma IL-6 did not prevent a substantial improvement in endothelial function with wine intake. Thus, overall, wine intake may have an acute beneficial effect on the vasculature that may conceivably contribute to the decreased risk of CHD associated with regular, moderate wine intake in epidemiologic studies. However, in the light of potential adverse effects of alcohol consumption and in the absence of a large, randomized, clinical end point trial of moderate wine intake in patients with CAD, use of wine (or alcohol) as a cardioprotective strategy cannot be recommended. Studies on the effects of drinking wine on plasma IL-6 levels and other markers of inflammation in healthy men and women and in women with CAD are warranted.

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