Dear Sir,

Moderate consumption of red wine is associated with lower incidence of cardiovascular disease, however, the source of this cardioprotective effect is still uncertain. Acute coronary syndromes are caused by atherosclerotic plaque rupture with ensuing platelet adhesion, aggregation and thrombus formation. Experimental studies in animals demonstrated that red wine inhibits platelet-dependent flow variation and mural thrombosis but the mechanism has not been fully clarified (1, 2). Even if ethanol inhibits platelet function, this effect is not achievable with moderate alcohol consumption (3); therefore, other mechanisms are likely to be implicated in the antithrombotic effect of moderate consumption of wine.

Much attention has been recently focused on the possibility that the cardioprotective effect of wine is dependent on polyphenols, its non-alcoholic component. This suggestion is supported by the existence of an inverse association between polyphenol intake and cardiovascular events (4). Polyphenols possess antioxidant property that could inhibit atherosclerotic lesion via inhibition of LDL oxidation and in turn cholesterol accumulation within the macrophages of atherosclerotic plaque (5). However, the antioxidant property of polyphenols could also modulate other aspects of the inflammatory process that are implicated in the pathogenesis of human atherosclerosis CD40 ligand (CD40L), a member of the tumor necrosis factor family, is a transmembrane protein with pro-inflammatory and pro-thrombotic properties upon interaction with its receptor CD40 (6). Engagement of CD40L with its receptor stimulates the synthesis of adhesion molecules, chemokines and tissue factor, and activates metalloproteinases (6). The role of CD40L in atherogenesis is confirmed by the fact that, in hyperlipidemic mice, anti-CD40L antibodies reduced the atherosclerotic lesion (7).

We have recently demonstrated that platelet production of $O_2^-$ has a key role in the expression of CD40L. Thus, in patients with hereditary deficiency of gp91phox, the central core of NADPH oxidase, platelet CD40L expression was prevented (7). On the basis of this finding we tested the hypothesis that polyphenols could prevent platelet CD40L expression via inhibition of platelet $O_2^-$ production. (n=5); SI= Stimulation Index, AU= Arbitrary Units. Student’s T test *P<0.01 vs untreated platelets.

Figure 1: Effect of scalar concentration of polyphenols on platelet $O_2^-$ and CD40L production (Panel A). Correlation between inhibition of $O_2^-$ and CD40L production in platelet treated with scalar concentration of Quercetin plus Catechin (Panel B). Collagen induced dose response curve in platelets treated with 5 uM quercetin or 25 uM catechin or 5 uM quercetin plus 25 uM catechin, Panel C CD40L expression, panel D platelet $O_2^-$ production. (n=5); SI= Stimulation Index, AU= Arbitrary Units. Student’s T test *P<0.01 vs untreated platelets.
subjects had taken antioxidants in the previous month; and they had refrained from consuming any alcoholic beverages in the two weeks prior to the study. Collagen-induced platelet $\alpha$-granule formation was measured by a chemoluminescence assay and expressed as stimulation index (SI) (7); collagen-induced platelet CD40L was measured by flow cytometry, values were expressed as arbitrary units (AU) (7). Platelets were incubated for 15 min at 37°C with the polyphenols quercetin (2.5–10 uM), catechin (12–50 uM), quercetin plus catechin, or the solvents as control before activation with collagen (1–16 ug/ml).

An amount of up to 10 uM quercetin or 50 uM catechin did not affect collagen (8 ug/ml)-induced platelet CD40L and $\alpha$-granule formation (Fig. 1, panel A). However, a combination of quercetin with catechin provoked a parallel inhibition of platelet CD40L and $\alpha$-granule formation, depending on the polyphenol concentrations (Fig. 1, panels A and B).

Using collagen <8 ug/ml, low concentrations of polyphenols were able to inhibit platelet CD40L and $\alpha$-granule formation but again, this effect was more marked if quercetin and catechin were combined (Fig. 1, panels C and D). Similar results were obtained with thrombin (0.1–1 U/ml) (data not shown).

This finding proves for the first time that polyphenols synergize in preventing platelet CD40L expression with a mechanism involving platelet production of $\alpha$-granules.

**References**


**Effect of compliance and dosage adaptation of long term aspirin on platelet function with PFA-100 in patients after myocardial infarction**

Dear Sir,

Low dose Aspirin® (ASA) reduces mortality in patients with previous myocardial infarction (MI) by 25% (1-3). However, the effect of aspirin may vary from patient to patient (4), and even in normals (5). Several studies demonstrated different frequencies of “aspirin resistance” (6-8) in different groups of patients. Moreover, the degree and type of aspirin resistance might have a significant effect on clinical outcome and antiplatelet therapy. Several papers have shown correlation between aspirin resistance and patient outcome. Since most studies are based on patients with long-term ASA-usage, compliance is often non-controlled. Also, different platelet function test systems are used in the respective studies. Both account for the wide variability found for aspirin resistance making a comparison of results almost impossible (9, 10).

We investigated if the frequency of “aspirin resistance” could be minimized by strictly reinforcing compliance, platelet function monitoring, and ASA dosage adaptation in patients with inferior platelet inhibition. This observational study aimed primarily at investigating whether these factors would show an ef-