Giuseppe (Joe) Mazza*

Scientific Evidence in Support of the Health Benefits of Wine

epidemiological evidence

Studies of wine and its effects on health have a long history, ranging from anecdotal accounts in ancient times to more recent rigorous studies of populations with hundreds of thousands of participants (Rimm et al., 2002; de Gaetano et al., 2002). Most studies suggest that men and women who drink 1 to 2 drinks per day on average have lower total mortality rates, reflected in lower incidence of coronary heart disease (Di Castelnuovo et al., 2002), diabetes (Ajani et al., 2000, Wannamethee et al., 2003.), ischemic stroke (Reynolds et al., 2003) and in some populations prostate cancer (Schoonen et al., 2005) and dementia (Mukamal et al., 2003).

Evidence from a recently published meta-analysis of 13 studies (involving 209,418 subjects) on the relationship between wine consumption and risk of cardiovascular disease (CVD) has revealed an average significant reduction of 32% of overall vascular risk associated with moderate (1-2 drinks or 150-300 mL/day) versus no wine consumption (Di Castelnuovo et al., 2002).

in vitro and *in vivo* studies

A second type of evidence that continues to emerge includes in vitro studies, studies in animal models of human disease, and measures of surrogate markers of disease in humans. Thus, a series of *in vitro* and *in vivo* studies suggest that

* *Pacific Agri-Food Research Centre, Summerland, British Columbia, Canada*

the polyphenolic compounds in red wine, in addition to ethanol, may play an active role in limiting the initiation and progression of atherosclerosis.

In in-vitro studies with phenolics in red wine and normal human low-density lipoprotein (LDL) showed that red wine inhibits the copper-catalysed oxidation of LDL (Frankel et al., 1993). Two possible mechanisms for this action were advanced, i.e., that phenolic compounds complex with Cu++ to reduce it to Cu+, which may in turn reduce hydroperoxides, and that during the LDL peroxidation, phenols in wine may act as self-regenerating reducing compounds. Therefore, these authors concluded that with regular ingestion of these antioxidant phenols via red wine consumption, a collective reduction in the oxidation of lipoproteins may occur and thus contribute to reduced atherosclerosis and morbidity and mortality from CVD.

Grape flavonoids also protect and increase serum HDL paroxonase by reducing macrophage oxidative stress through inhibition of cellular oxygenases such as NADPH oxidase, or myeloperoxidase (Fuhrman and Aviram, 2001).

From a comparison of *in vitro* effects of red wine, white wine and ethanol on cell mediated oxidation of LDL and HDL by three frequently-used assays Vincent et al. (1999) reported that red wine (0.2 mg ethanol/mL) inhibited LDL oxidation as indicated by an 85.7% decrease in absorbance at 234 nm, a 96.5% decrease in TBARS production and complete prevention of the decrease in TNBS reactivity. White wine and ethanol did not have any significant effect at 0.2 mg/mL. White wine at 1.0 mg ethanol/mL inhibited TBARS production from LDL by 84.1%. Red wine (0.2 mg ethanol/mL) inhibited HDL oxidation as indicated by a 78.9% decrease in $\Delta A234$, an 81.7% decrease in TBARS production and by no change in TNBS reactivity. The authors concluded that red wine inhibits the cell mediated oxidation of lipoproteins, that white wine is not as effective as red wine and that the effect of the red wine is not due to its ethanol content.

Numerous studies with dogs, monkeys, rabbits and hamsters have shown that red wine may inhibit the initiation of atherosclerosis by one or more of the following mechanisms: platelet activation, oxidative modification of LDL, endothelial dysfunction, and inflammation (Folts, 2002).

CONTROLLED CLINICAL TRIALS

Recently, Tsang et al. (2005) investigated the effects of moderate red wine consumption on the antioxidant status and indices of lipid peroxidation and oxidative stress associated with CHD. They performed a randomised, controlled study with 20 free-living healthy volunteers in which subjects in the red wine

group consumed 375 mL red wine (young vatted Cabernet Sauvignon, 12% alcohol) daily for 2 weeks, and measured the total concentration of phenolics and analysed the individual phenolics in the wine and plasma by HPLC with tandem MS. The antioxidant capacity of plasma was measured with electron spin resonance spectroscopy while homocysteine and fasting plasma lipids were also determined. The production of conjugated dienes and thiobarbituric acid-reactive substances (TBARS) were measured in Cu-oxidised LDL. Plasma total phenolic concentrations increased significantly after 2 weeks of daily red wine consumption ($P < 0.001$) and trace levels of metabolites, mainly glucuronides and methyl glucuronides of (+)-catechin and (-)-epicatechin, were detected in the plasma of the red wine group. These flavan-3-ol metabolites were not detected in plasma from the control group. The maximum concentrations of conjugated dienes and TBARS in Cu-oxidised LDL were reduced ($P<0.05$) and HDL cholesterol concentrations increased ($P<0.05$) following red wine consumption. These findings provide some evidence for potential protective effects of moderate consumption of red wine in healthy volunteers.

A randomized, crossover, single-blind trial by Estruch et al. (2004) evaluated the effects of wine and gin on inflammatory biomarkers of atherosclerosis. Forty healthy men (mean age, 37.6 years) consumed 30 g ethanol per day as either wine or gin for 28 days. Before and after each intervention, they measured the expression of lymphocyte function-associated antigen 1 (LFA-1), Mac-1, very late activation antigen 4 (VLA-4), and monocyte chemoattractant protein (MCP-1) in monocytes, as well as the soluble vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), interleukin-1α (IL-1α), C-reactive protein (hs-CRP) and fibrinogen. The results showed that after either gin or wine consumption, plasma fibrinogen decreased by 5 and 9%, respectively, and cytokine IL-1α by 23 and 21%. The expression of LFA-1 (–27%), Mac-1 (–27%), VLA-4 (–32%) and MCP-1 (–46%) decreased significantly after wine, but not after gin. Wine reduced the serum concentrations of hs-CRP (–21%), VCAM-1 (–17%) and ICAM-1 (–9%). Thus, both wine and gin showed anti-inflammatory effects by reducing plasma fibrinogen and IL-1α levels. However, wine had the additional effect of decreasing hs-CRP, as well as monocyte and endothelial adhesion molecules.

OTHER HEATH EFFECTS

In addition to the negative association between wine/alcohol consumption and mortality from coronary heart disease that has now been observed in

many studies, some epidemiological studies have associated alcohol or wine consumption with reduced rates of incidence of several other diseases. These include prostate cancer (Schoonen et al. 2005), diabetes (Ajani et al. 2000, Wannamethee et al. 2003.), ischemic stroke (Reynolds et al. 2003), and dementia and Alzheimer's disease (Mukamal et al. 2003).

CONCLUSIONS

Epidemiological studies and recent *in vitro* and *in vivo* data indicate that moderate daily intake of wine (1-2 drinks a day) may reduce the risk of developing CHD and stroke. Other positive effects of wine on health such as decreasing the risk of certain cancers and Alzheimer's disease remain to be established. Red wine, which has a higher content of phenolics appears to be superior to white wine and other alcoholic beverages protecting against CHD and stroke. However, in this era of evidence-based medicine, a large-scale randomized control trial, assessing the effects of red wine intake versus a non-alcoholic placebo, would be required to ensure that there is legitimacy to both the epidemiological and biological data. Only based on the favourable results of such a study may health professionals be fully justified in recommending the consumption of red wine for cardiovascular protection. In the mean time, my advise is to drink wine moderately to health, and perhaps for health!