# Wine polyphenols and heart health

**Dr Karen Cooper**

## World wine consumption

For the last 6,000 years, the drinking of wine has been a part of human culture. Since that time, wine consumption has been recorded in various countries as part of their traditions and dietary choices, with the Mediterranean areas appearing to enjoy better health as a consequence of their lifestyle (see Figures 1a and b).[1-3]

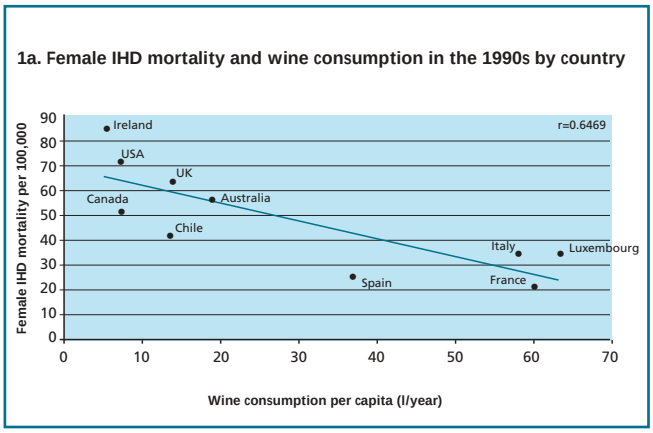
The French paradox is the well-known term to describe an unexpected finding of the MONICA Project.[4] France was shown to have coronary mortality close to that of China or Japan in spite of saturated fat intake and plasma cholesterol concentrations similar to the UK and US. Wine consumption was suggested as a possible protective factor.[5] However, the time-lag hypothesis cast doubt on this explanation.[6] The latter hypothesis observed that high animal fat consumption and serum cholesterol levels have only been similar between France and Britain since the mid-1980s. Before this time, the levels of animal fat consumption (~21% of total energy consumption in France versus ~31% in Britain) and mean serum cholesterol (5.7 versus 6.3mmol/l) in men aged 50-70 years were lower in France than in the UK.[4,7] Therefore, the new hypothesis suggests that changes will occur in the pattern of coronary heart disease (CHD) in France, with increases in atheroma and deaths from CHD within the next 25-35 years.

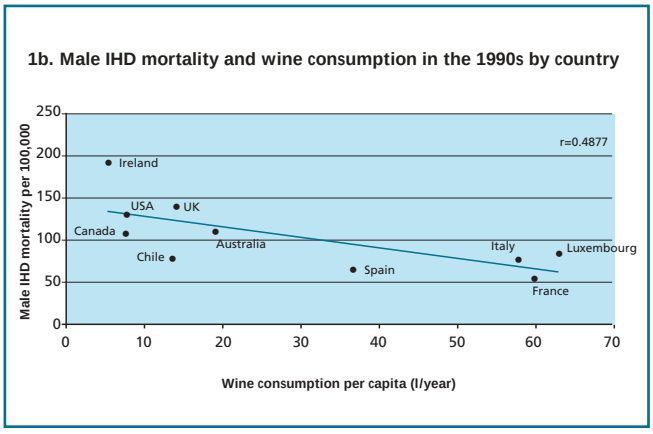
## Polyphenols in wine

Polyphenols in wine originate mainly from the skin and seeds of the grape but can also be derived from the vine stems, the wood used for barrels and from yeast metabolism.[8] Polyphenols can be split into two groups: flavonoids and non-flavonoids. Flavonoids are the most common and widely distributed group of phenolics, some of which are described here.[9]

The flavonoid group can be further broken down into subclasses. Flavonols are antioxidant polyphenols such as quercetin, myricetin and kaempferol and are found in a wide variety of foods, e.g. leeks, broccoli, onion, lettuce, cranberries, apples, olives and beverages such as tea and red wine. Flavonols or catechins are more popularly associated with tea and chocolate rather than wine, but there are higher concentrations of catechins in red wine than all the other flavonoid compounds.[10] Procyanidins are oligomeric structures that can occur in a wide range of concentrations in red wine and also cocoa products. Resveratrol is found in grape skin and is known to be one of the primary active components in the Oriental folk medicine for atherosclerosis 'Kojo-kon' or 'Itadori-kon'.[11]

Non-flavonoid components of wine are simple abundant phenols with a variety of different functional groups present. Wine astringency is attributed to the presence of the larger polyphenols and the smaller phenolic acids account for bitterness. Volatile phenols can contribute to wine characteristics such as smokiness, vanilla character, pungency and bitterness but these components are usually only present in tiny amounts.[12]




Figures 1a and b. Mortality and wine consumption in (a) females and (b) males in the 1990s by country. Source: The Wine Institute. Per capita wine consumption by country in litres and gallons per capita (www.wineinstitute.org), 1999.

## Is it the alcohol?

One question, still not answered, is whether the apparent cardioprotective effects associated with wine consumption stem from the alcohol, other wine components or a mixture of the two. Alcohol intake, in general, is inversely correlated to the risk of CHD but the link with wine alcohol specifically is stronger than

beer alcohol and more consistent. Consumption patterns such as wine drinking with meals or daily versus weekend binge drinking are important aspects when reporting epidemiological links between alcohol consumption and CHD risk.

## Effects of wine on risk factors for CHD

### Lipids

In general, supplementation trials of red and white wine are designed to allow observation of short-term changes that may be indicative of long-term protection against CHD, for example, of plasma lipids. Typically, the trials supplement with 200-500ml/day for approximately two weeks, but some for as long as four weeks. Longer trials are not generally performed as effects are seen within weeks on plasma lipids, and the ethics of supplementing alcoholic beverages for long periods of time must be considered. Overall, studies indicate that red wine consumption is effective in only increasing HDL concentrations. The lack of effect from the grape juices and the positive result from the white wines and non-phenolic alcoholic beverages suggest that alcohol in these cases was the most probable factor causing the effects on HDL.

The results from studies to determine the effects of wine supplements on susceptibility of LDL to peroxidation are mixed and appear to be dependent on trial conditions. Alcohol may be needed to act synergistically with the wine phenolics or potentially aid absorption into the bloodstream.[13] Evidence has been found to suggest that long-term and regular consumption of red wine, but not alcohol, can inhibit LDL oxidation *ex vivo*.[14] Comparisons have been made between the modes of administering the red wine polyphenols.[15] The study showed a protective effect of red wine itself and an extract of its polyphenols against LDL peroxidation but the effect of the latter seemed to depend on whether it is presented in an alcoholic medium.

There is a possibility that the protective effects of wine polyphenols may only be observed in hyperlipidaemic subjects.[16] A high plasma lipid level allows more lipid to be available for oxidative modification by free radical species; therefore, hyperlipidaemia can lead to increased oxidative damage.[17] Most studies reported in the literature were performed with normolipidaemic subjects and thus potential benefits from wines may have been marginal and not significant. Subjects with elevated lipid status or in a disease state where oxidative damage is being caused may have a more pronounced response to polyphenol supplementation.

### Serum antioxidant capacity

Increased antioxidant activity has been linked to the consumption of red wine, but not white wine. Single doses of red wine (113ml of alcohol-free and 300ml of alcohol-containing wine) were effective within an hour of consumption.[18,19] Consumption of 300ml of alcoholised red wine was still effective after four hours.[20] Grape juice was also effective within an hour of consumption, and this was maintained and increased after seven days of supplementation.[21] Thus, polyphenols supplemented *in vivo* in different forms, i.e. wine and grape juice, all had a positive effect on serum antioxidant capacity.

These studies appear to indicate that the effective component in this case might not be alcohol but rather polyphenol concentration. The effects of grape juice may not be completely analogous to the non-alcoholic content of red wine, as grape juice does not contain flavonoids from the skin and seeds of the grape whereas red wine does.

### Vasculature

Endothelial dysfunction is linked to many of the risk factors for CHD including hypercholesterolaemia, smoking and familial history of premature CHD. In addition, many coronary risk factors are known to reduce nitric oxide (NO) availability, making NO a popular intermediate end-point for assessing atherogenic risk.[22] Control of vascular relaxation is endothelium-dependent and is mediated by NO.[23] The presence of wine with a diet has been shown to prevent fat-related changes in endothelial function. In the absence of wine, high fat diets (39.5% of total calories) in six volunteers depressed function (-2.9% ± SD 2.1) when compared with a diet containing fat as only 27% of total calories where the change was +3.1% ± SD 3.9.[23] This difference was not observed when 240ml/day of red wine was supplemented with both high fat (6.6% ± SD 2.2) and control (5.8% ± SD 4.6) diets.

A few studies have also investigated possible links between blood pressure and polyphenol consumption. One study found a decreased blood pressure with a phenolic beverage (grape juice and vinegar mix) in rats.[24] Similar effects have been seen with supplementation with single phenolics such as ferulic acid in hypertensive rats.[25]

### Platelets

Platelet aggregability is an important factor in CHD. *In vitro*, alcohol has a similar effect to aspirin in its ability to decrease secondary aggregation of platelets in response to adenine diphosphate (ADP). A suggestion has been made that as wine is generally consumed with food, the alcohol is absorbed slowly; therefore, it can have a longer effect on the body's metabolism, e.g. on blood platelet reactivity at a time when lipid levels would be high.[5] *In vivo* inhibition of platelet aggregation by moderate alcohol consumption was noted in the Caerphilly Prospective Heart Disease study[26] and, later, in an acute consumption study when both platelet-rich plasma and whole blood were examined.[27]

Both wine and grape juice can affect platelet aggregation in humans, by reducing plasma thromboxane $B_2$ ($TxB_2$) concentration and the concentration of ADP and thrombin available for platelet aggregation. One study found that red wine ingestion reduced but surprisingly pure alcohol increased platelet aggregation.[28] It was suggested that this effect was due to the presence of aspirin in red wine, but red wine has been shown to contain only negligible amounts of aspirin.[29] Supplementation studies have shown that platelet aggregation was strongly inhibited by red wine, moderately inhibited by grape juice and unaffected by white wine. Overall, the effects of alcohol on platelet aggregation appear to be enhanced by wine or grape polyphenols.

## Conclusion

Wine has been part of human culture and diet for many thousands of years and will probably continue to be so for many more to come. In spite of tremendous research input in

this area in the past decade, we still have a great distance to cover in our understanding of the health benefits of wine. Although we know a lot more about the phenolic components of red wine, we still do not know whether the components have individual functions and which are the most important.

Future research is likely to be directed into the areas concerning the biological activities of phenolics and their metabolites at cellular, molecular and biochemical levels.

## References


1. Trichopoulou A, Kouris-Blazos A, Vassilakou T et al. Diet and survival of elderly Greeks: a link to the past. *Am J Clin Nutr* 1995; 61: 1346S-50S.
2. Willett WC, Sacks F, Trichopoulou A et al. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr* 1995; 61: 1402S-6S.
3. Kushi LH, Lenart EB, Willett WC. Health implications of Mediterranean diets in light of contemporary knowledge. 2. Meat, wine, fats and oils. *Am J Clin Nutr* 1995; 61: 1416S-27S.
4. The WHO MONICA Project. A worldwide monitoring system for cardiovascular diseases: cardiovascular mortality and risk factors in selected communities. *World Health Statistics A* 1989: 27-149.
5. Renaud S, de Lorgeril M. Wine, alcohol, platelets, and the French paradox for coronary heart disease. *Lancet* 1992; 339: 1523-6.
6. Law M, Wald N. Why heart disease mortality is low in France: the time lag explanation. *BMJ* 1999; 318: 1471-80.
7. Crique MH, Ringel BL. Does diet or alcohol explain the French paradox? *Lancet* 1994; 344: 1719-23.
8. Soleas GL, Diamandis EP, Goldberg DM. Wine as a biological fluid: history, production, and role in disease prevention. *J Clin Lab Anal* 1997; 11: 287-313.
9. Bravo L. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutr Rev* 1998; 56: 317-33.
10. Goldberg DM, Karumanchiri A, Tsang E, Soleas GL. Catechin and epicatechin concentrations of red wines: regional and cultivar-related differences. *Am J Enol Viticulture* 1998; 49: 23-34.
11. Lamuela-Raventós RM, Waterhouse AL. Resveratrol and piceid in wine. *Methods Enzymol* 1999; 299: 184-90.
12. Singleton VL. Grape and wine phenolics; background and prospects. AD Webb. Proceedings of the University of California, Davis, pp 215-27. 1982. Davis, US, University of California Press. Grape and Wine Centennial Symposium.
13. de Rijke YB, Demacker PNM, Assen NA et al. Red wine consumption does not affect oxidisability of low density lipoproteins in volunteers. *Am J Clin Nutr* 1996; 63: 329-34.
14. Kondo K, Matsumoto A, Kurata H et al. Inhibition of oxidation of low density lipoprotein with red wine. *Lancet* 1994; 344: 1152.
15. Nigdikar SV, Williams NR, Griffin BA, Howard AN. Consumption of red wine polyphenols reduces the susceptibility of low-density lipoproteins to oxidation in vivo. *Am J Clin Nutr* 1998; 68: 258-65.
16. Chopra M, Thurnham DI. Antioxidants and lipoprotein metabolism. *Proc Nutr Soc* 1999; 58: 663-71.
17. Prasad K, Kalra J. Oxygen free radicals and hypercholesterolaemic atherosclerosis – effect of vitamin E. *Am Heart J* 1993; 125: 958-73.
18. Serafini M, Maiani G, Ferro-Luzzi A. Alcohol-free red wine enhances plasma antioxidant capacity in humans. *J Nutr* 1998; 128: 1003-7.
19. Whitehead TP, Robinson D, Allaway S et al. Effect of red wine ingestion on the antioxidant capacity of serum. *Clin Chem* 1995; 41: 32-5.
20. Cao G, Russell RM, Lischner N, Prior RL. Serum antioxidant capacity is increased by consumption of strawberries, spinach, red wine or vitamin C in elderly women. *J Nutr* 1998; 128: 2383-90.
21. Day AMP, Kemp HJ, Bolton C et al. Effect of concentrated red grape juice consumption on serum antioxidant capacity and low density lipoprotein oxidation. *Ann Nutr Metab* 1997; 41: 353-7.
22. Vogel RA. Vintners and vasodilators: are French red wines more cardioprotective? *J Am Coll Cardiol* 2003; 41: 479-81.
23. Cuevas AM, Guasch V, Castillo O et al. A high fat diet induces and red wine counteracts endothelial dysfunction in human volunteers. *Lipids* 2000; 35: 143-8.
24. Sugiyama A, Saitoh M, Takahara A et al. Acute cardiovascular effects of a new beverage made of wine vinegar and grape juice, assessed using an in vivo rat. *Nutr Res* 2003; 23: 1291-6.
25. Suzuki A, Kagawa D, Fujii A et al. Short- and long-term effects of ferulic acid on blood pressure in spontaneously hypertensive rats. *Am J Hypertens* 2002; 15: 351-7.
26. Renaud S, Beswick AD, Fehily AM et al. Alcohol and platelet aggregation: the Caerphilly Prospective Heart Disease study. *Am J Clin Nutr* 1992; 55: 1012-7.
27. Zhang Q-H, Das K, Siddiqui S, Myers AK. Effects of acute, moderate ethanol consumption on human platelet aggregation in platelet-rich plasma and whole blood. *Alcohol Clin Exp Res* 2000; 24: 528-34.
28. Seigneur M, Bonnet J, Dorian B et al. Effect of the consumption of alcohol, white wine and red wine on platelet function and serum lipids. *J Appl Cardiol* 1990; 5: 215-22.
29. Janssen PLTMK, Katan MB, Hollman PCH, Venema DP. No aspirin in red wine. *Lancet* 1994; 344: 762.



**This article is based on work carried out at the Northern Ireland Centre for Food and Health (NICHE), University of Ulster, Coleraine, Northern Ireland.**

**Dr Karen Cooper PhD, MSc currently works at the Department of Nutrition and Health, Nestlé Research Centre, Lausanne, Switzerland.**