



dr paul clayton's

Health Newsletter

Winter 2008

Jetlag
Red Wine
Lifestyle

Seasons, seasonings and jetlag

We are rapidly approaching what is traditionally known as the season of good cheer. Unfortunately, Christmas 2008 will not be as cheerful as usual for many, thanks to the greed and stupidity of our financial and political masters who are herding us into the black hole of a near-global depression. All the more need, then, for a little good news from the alternative world of nutrition; so this time I will focus on the health benefits that are increasingly being linked to red wine.

Drink up, and try to forget that while we may be lions, we are manifestly led by donkeys.

Jetlag - pycnogenol, flavonoids, melatonin

For an entree, consider the interesting news that pycnogenol, a mixture of flavonols and flavonoids derived from French maritime pine bark, may be able to reduce jet lag in passengers taking long haul (7 to 9 hour) flights (Belcaro et al '08). The two-part study, which was conducted at G. D'Annunzio University in Pescara, incorporated a brain CT scan and a comprehensive scoring system.

A total of 133 passengers were given 50 mg of pycnogenol three times daily for seven days, starting two days prior to the flight. In the first part of the study, thirty-eight pycnogenol-treated and 30 control patients were rated on the common complaints of jetlag including: dehydration, loss of appetite, fatigue, insomnia and/or highly irregular sleep patterns, reduced mental performance and general well-being. The total jetlag score was halved in the treated group, and the duration of the symptoms was also halved.

In the second part of the study, 34 pycnogenol-treated patients and 31 control patients were given brain CT scans to assess changes in brain structure and function; and here, the extract halved the slight degree of brain edema (swelling) that can occur during long-haul flights. The researchers concluded: "Pycnogenol is emerging as a natural, yet safe option for long distance travellers."

I am not terribly impressed by this study. Pycnogenol is just one (over-priced) proprietary brand of flavonoids and

flavonols, compounds which occur in a very wide variety of plant foods. You will find them, for example, in tea, coffee,



apples, onions, and red wine – all of which taste better than pycnogenol, and the pine bark it is extracted from. If you are committed to a long-haul flight over the holidays, I would recommend you combine flavonoids with a supplement of melatonin, a fascinating compound which specifically re-sets the biological clock (Herxheimer & Petrie '02, Srinivasan et al '08).

Melatonin is so effective and so safe (when used to treat occasional jetlag) that the medical orthodoxy in the EU banned it from the supplement market; acting, it would appear, at the behest of a pharmaceutical company who wanted to have a clear run for their semi-synthetic version of melatonin. The American authorities have adopted a more enlightened attitude, and this invaluable supplement is available

over the counter in good health food shops across the USA.

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Wining - the antidote to Dining?

For the main course, a selection of good red wines – and their flavonoidal constituents, which have been linked to a very wide range of health benefits. Let us begin, perversely, with the liver. The incidence of liver disease is increasing remarkably, due to the dual insults of alcohol (which are of course well known) and metabolic syndrome/type 2 diabetes. The latter category of liver disease, known as Non-Alcohol-Related Fatty Liver Disease (NAFLD) has shown a spectacular increase. Almost unknown twenty years ago, NAFLD is now the most common liver disease in the US where it affects over 40 million adults, and is growing world-wide as nations become increasingly obese.

Until very recently, alcohol has been medically forbidden to those whose lifestyle has led to overweight, and type 2 diabetes. These people are already at risk of NAFLD, ran the reasoning, so they should avoid anything else that might cause liver damage. That common-sense concept, however, has now been contradicted by an interesting and large-scale study, carried out at the San Diego School of Medicine, on nearly 12,000 individuals (Dunn et al '08).

"The odds of having suspected NAFLD based upon abnormal liver blood tests was reduced by 50 per cent in individuals who drank one glass of wine a day", said senior author Professor Jeffrey Schwimmer, "and the result remained constant, even after adjusting for age, sex, race, education, income, diet, physical activity, body mass index, and other markers of health status."



MULBERRIES

What Schwimmer was saying here was that the result was likely to be a real one, and that wine is genuinely protective against NAFLD. This view was supported by the fact that in marked contrast to the wine drinkers, people who reported modest consumption of beer or spirits had over four times the risk of having suspected NAFLD. In other words, alcohol per se is not good for the liver (which we all knew); but wine contains something that confers an overall benefit.

Previous research has linked the health benefits of wine to **resveratrol**, a flavonoid that occurs naturally under the skin of red wine grapes. Resveratrol has been associated with the so-called 'French Paradox', a phrase used to describe the unfairly low incidence of heart disease and obesity among the French, despite their relatively high-fat diet and levels of wine consumption.

The San Diego study did not attempt to look at the mechanism whereby resveratrol might be protecting the liver, but many other scientists are working with this valuable molecule. In one very provocative experiment, resveratrol appeared to be so good for the liver that it conferred strong protection against alcohol-induced damage, albeit in a mouse model (Ajmo et al '08). The authors measured a positive impact of resveratrol on a wide range of biomarkers for liver function and concluded that "resveratrol may serve as a promising agent for preventing ... human alcoholic fatty liver disease."

The mouse is not always an accurate animal model, but several of the mechanisms whereby resveratrol protect the liver, including up-regulation of the important gene Sirtuin-1 (Pfluger et al '08), are common to both mice and men. This gene would be expected to reduce the risk of a number of diseases, and could help to explain why wine drinking is linked to a reduced risk of lung cancer (Prescott et al '99, Cho '07), gastric cancer (Barstad et al '05), certain types of colorectal cancer (Zell et al '07), heart disease (Groenbaek et al 2000) – and indeed, death from all causes (Groenbaek et al '95, Renaud et al '04). In marked contrast, beer and spirits either have no protective effect, or confer increased risk.

To back this up, resveratrol and other compounds found in grapes and in wine have been shown to kill a wide range of cancer cells (ie Engelbrecht et al '07, Kaur et al '08, Okunieff et al '08). Some have said that the cancer-killing effects of resveratrol noted in these studies occurred at extremely high (ie non-dietary) levels, but that may not be relevant.

To begin with, pure resveratrol is now known to mimic many of the anti-ageing effects of calorie restriction at doses not too far outside the current human dietary range (ie Pearson et al '08, Barger et al '08), and within the historical dietary range (Rowbotham & Clayton '08). To make matters even more biologically relevant, it is becoming apparent that whereas the pharmaceutical model would

prefer to deal with pure resveratrol, its protective effects are greatly enhanced by other compounds present in whole foods. For example, one recent study demonstrated that low doses of grape powder are in fact very good at switching off cancer genes in patients with colorectal cancer (Holcombe et al '07). Watch this space!

NB. The amount of resveratrol in a bottle of red wine depends on the types of grapes and the growing seasons, and can vary between as little as 0.2 and as much as 15 milligrams per litre (Stervbo et al '07). As a rule of thumb, the darker red wines contain generally higher levels of resveratrol and all the other flavonoidal compounds. Other excellent sources of resveratrol include **raspberries, mulberries, peanuts and blueberries**.

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Lest we forget ...

For dessert, a few more flavonoids; because as well as all the above benefits, they may protect against Alzheimer's disease too.



Alcohol – especially wine – is associated with a reduced incidence of dementia and Alzheimer's (ie Baranco-Quintana et al '05, Luchsinger et al '07); but is this association meaningful? Would wine, for example, work as a prophylactic?

In a recent study, a research team at Mount Sinai School of Medicine study found that giving cabernet sauvignon wine to mice prone to growing amyloid plaque in their brains (a model for Alzheimer's) prevented the formation of amyloid plaque, and slowed the associated memory loss and brain cell death (Wang et al '06, Ono et al '08).

Flavonoids extracted from wine were equally protective (Ono et al '03), but alcohol alone had no effect. The findings were made more interesting by the fact that here again, a low dose of wine was enough – ie no more than a glass or two per day.

Add a spoonful of **turmeric**, which contains similar compounds, and you will probably gain additional protection (ie Kim et al '05).



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Dont' cry into your beer, Argentina

All the good news about wine must seem irrelevant to beer drinkers, but I can now announce the forthcoming release of a beer designed to convey the health benefits of wine. This should happen sometime in the next three years, IF the regulators let it though.

Scientists at Rice University in Houston, Texas, are currently working with a local brewer to develop yeast that can produce resveratrol, and the Danish company Fluxome has already developed a strain of yeast that produces significant amounts of the same compound. This may well move the beers of the future (like red wine) into the health food category; but I cannot resist passing on the fact that beer already contains a functional compound called **xanthohumol**.

Xanthohumol is derived from hops, and is yet another flavonoid. Like resveratrol, xanthohumol has anti-inflammatory (Cho et al '08) and anti-cancer effects (ie Ho et al '08, Monteghirfo et al '08, Monteiro et al '08). It even has antibiotic effects! (Natarajan et al '08)

I am not recommending excessive alcohol consumption as a route to better health. I merely point out that beer, like wine, is not entirely bad, and is a valuable piece in any dietary jigsaw. And as always, drink responsibly.



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The American way we live now

I have written before about the way in which the degenerative diseases are not an inevitable part of ageing. They are largely caused by the way we live, and history shows us that they are very much a product of the urbanised 20th and 21st centuries.

The corollary, of course, is that these diseases can generally be prevented by simple diet and lifestyle changes. Regular readers of my newsletters, and many others who take a constructive approach to their own health, are already undoubtedly enjoying the benefits, but we remain a small and relatively insignificant group.

At the level of the general population, things are getting worse – and in the absence of any coherent and sustained strategy from governments, doctors and educators, most of whom are still hopelessly in hock to the drug model of health – the situation will continue to deteriorate.

In October, for example, a report from the US Centers for Disease Control and Prevention (CDC) revealed that the numbers of people with Type 2 diabetes has increased by 90% – in other words, almost doubled – in the last ten years alone (CDC '08).

Specifically, the incidence of Type 2 diabetes increased from 4.8 people per 1,000 in 1995-1997 to 9.1 people per thousand in 2005-2007. This is likely to be an under-estimate, as the data was mined from self-reported surveys. About a third of diabetics do not know they are diabetic, and so the real figure is probably around 14 to 15 people per thousand.

There is a strong north-south gradient in the US for diabetes, with the highest incidence noted in the South. In the CDC report, the clinical scientists took the view that the diabetes pandemic is due in the main to obesity; but the fact that obesity is an all-American problem (CDC '07), while Southern citizens are nearly twice as likely to be diabetic, indicates that obesity is not the only factor.

It is true that three Southern states (Alabama, Mississippi and Tennessee) have the highest obesity rates of over 30%, but 27 other states have obesity rates over 25%, and the CDC's own

obesity maps show no north-south gradient (CDC '07).

Despite educational and political differences, the ten highest annual diabetes rates are in ten geographically southern states:



Alabama, Florida, Georgia, Kentucky, Louisiana, South Carolina, Tennessee, Texas, West Virginia and Arizona.

And here we can see another possible common factor: these states are so hot for much of the year that most folks do not walk or take much physical activity of any form out of doors. The problem is exacerbated by (relatively) cheap petrol and poor urban design. Houston and Dallas, for example, are cities almost devoid of sidewalks (pavements), making it almost impossible to move around except by car.

And now we are getting to the heart of the problem. We evolved as highly active hunter-gatherers, and our bodies are designed for a high-energy lifestyle. If our muscles are not trained, they become insulin-resistant (Fosgerau et al '06, Muoio & Koves '07), and this, combined with our high intakes of sweet and starchy foods, is what is driving the diabetes pandemic both in the USA, and here in the 51st state.

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The "cure" for cardio-vascular disease

Don't smoke, maintain normal bodyweight, take regular exercise, drink in moderation, eat a Mediterranean diet. It is generally agreed that if you follow these recommendations you will be relatively free of cardiovascular disease. But can we be more precise? Can we, for example, look at mechanism, ask which dietary constituents are most cardio-protective, and then focus on them to reduce the risk still further?

There are clearly certain foods which should be **minimised or avoided**, as they contain excessive amounts of pro-inflammatory compounds. As these tend to be produced by high-temperature cooking (ie Negrean et al '07), many of the so-called **fast foods**, particularly those which are grilled or deep-fried, are in the frame. **Salty foods**, which inevitably lead to increased blood pressure (Wu et al '98, Karpunen & Mervaala '06), should also be minimised.

There are, equally clearly, certain foods with **cardio-protective properties**. These have one thing in common,

namely **flavonoids**, anti-inflammatory compound which target the blood vessels.

The flavonoids in **tea**, for example, have been shown in a series of clinical trials to improve arterial endothelial function (Widlansky et al '07), and to reduce inflammation markers and blood pressure (Nantz et al '08). Similar flavonoids in **onion** and **apples** have identical effects (Edwards et al '07, Tribolo et al '08, Lodi et al '08, Loke et al '08). Related flavonoids in hibiscus tea and in **cocoa** have the same benefits (Ajay et al '07, Balzer et al '08, Sorond et al '08).

How much should we eat? It is difficult to be precise, but it is probably best to aim for a dose that is towards the top of the dietary range. Intakes today are at an historic low, so I prefer to use as my frame of reference the mid-Victorian diet, which is strongly associated with a near-immunity to heart disease (Rowbotham & Clayton '08).

For References, please see www.drpaulclayton.com.

The Paul Clayton Newsletter describes developments in the new field of pharmaco-nutrition, where nature and science are combined to offer non-drug solutions to degenerative disease. The Newsletters are intended to increase knowledge and awareness of health issues and are for information only. No health claims for specific products are made or intended and the information should not be used as a substitute for medical advice.