AIM Alcohol in Moderation

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Antioxidants - never out of the news

Who could have failed to see the myriad of front page leaders around the world dedicated to the virtues of resveratrol and procyanidins in red wine (and dark chocolate) following two research articles published in Nature (Corder R, Crozier A et al 'Red wine procyanidins and vascular health' and Baur JA et al 'Resveratrol improved health and survival of mice on a high calorie diet'). Indeed, the research was the most widespread story reported in the world that day - with journalists apparently elated, in the run up to Christmas, that a little of those 'naughty' things in life are not only enjoyable, but positively not bad for you. The publicity has led to a surge of red wine sales in the US to twice their expected growth rate in November.

It is important to keep such publicity in proportion as an industry or indeed as consumers. No one should be choosing to drink for 'medical benefits' rather than enjoyment and pleasure. Secondly, it is not deemed acceptable for producers to promote or market their products as antioxidant-rich (which can by applied to traditional beers and ciders, even whisky as well as red wine) or as a health drink. In this era when many are seeking a universal panacea, there is no better alternative to the five 'ingredients' to a longer and healthier life - namely staying slim, eating a Mediterranean-style diet, exercising for 20 minutes daily, not smoking and drinking in moderation.

Such head lines are important in the sense that they do reinforce the 'rights' of moderate drinkers in that alcohol can be included as part of a healthy diet and lifestyle.

Some critics have stated that the continuing good news for red wine drinkers will encourage those at risk of a heart attack or a second heart attack to drink more or above daily sensible drinking guidelines and it is worth revisiting Professor Klatsy's work in this field. In 'Do people drink more if they develop Coronary Heart Disease (CHD) or know about medical benefits of alcohol' (AIM Vol 13 No.1 Jan 2004), Klatsky's subjects were drawn from 63,000 subjects in 1999, drawing on their drinking information supplied between 1978 and 1985. The analysis in 2000, found that 92% of the participants remained abstainers 20 years after first analysis, although 82% of the participants had heard of the medical benefits of alcohol. Of those who had contracted CHD, 18% had become abstainers, the same proportion as in the control, and more had given up smoking. Klatsky's findings concluded that knowledge of alcohol's potential beneficial effect did not alter patients drinking habits.

Antioxidants revisited:

Antioxidants include naturally occurring vitamins, phenolic compounds or other complex molecules generated by heat (i.e. cooking) such as elanoidins.

Resveratrol, along with quercetin and epicatechin, is one of the main antioxidants found in wine. These phenolic bioflavonoid compounds, a group of chemicals called phytoalexins, are produced by plants in response to fungal infection, ultraviolet light, and various chemical and physical stressors, especially during ripening. Dr Edwin Frankel, of the Davis University of California, has shown that these antioxidants in wine are five times more potent as antioxidants than the benchmark antioxidant, vitamin E.

Antioxidants are not exclusive to grapes, and are also found in, for example, allium vegetables (onion, leek, garlic, shallot), broccoli, spinach, blueberries, strawberries, tea and chocolate. It should be noted that antioxidants cannot be stored by the body like vitamins, so the protective antioxidant effect only lasts a few hours, hence we need to eat fruit and vegetables daily for their antioxidant content.

Antioxidants act in addition to the alcohol itself. Alcohol in moderation contributes at least half of wine's cardiovascular benefits. It also may enhance the desired actions of the antioxidants, and aid their absorption and bioavailability.

Potential actions of antioxidants

Reducing LDL oxidation

Enhancing vasodilation (endothelial function)

Anti-atherogenic effects

Shielding DNA from oxidative damage (oxidation may be promoted by acetaldehyde)

Modulating carcinogenic infllatory reactions

Promoting normal cell differentiation and maturation

Inhibiting growth of cancer cells and stimulating 'programmed cancer cell death'

Enhancing the effects of chemotherapy

Stimulating gene SIRT 1 which reduces development of new fat cells and increases the metabolism of fat in existing fat cells

Anti fibrotic properties which inhibit cardiac fibroblast proliferation

Antibiotic properties against heliobacter pylori

Increase levels of the enzyme heme oxygenase in the brain that shields nerve cells from damage

Role of antioxidants:

One of the main actions of antioxidants is to inhibit low density lipoprotein(LDL) or bad cholesterol from entering blood vessel walls and forming antheromatous plaques which eventually block off arteries causing vascular diseases such as heart attack and stroke. As we absorb polyphenols they change the properties of blood lipids making 'bad' LDL more resistant to oxidation and help 'relax' blood vessel walls, making blood flow easier.

Antioxidants can be many different compounds but they all share one property in that they are able to quench, or neutralise oxidative free radicals. In theory, the more antioxidants in your cells, the less free radicals. This is important because it is free radicals which are suspected to be involved in cancer development and in speeding up the progression of cardiovascular disease.

Free radicals are negatively charged rogue molecules (with one unpaired electron in their orbit). The body is continuously producing waste products from its many complex bio chemical pathways. These waste products include free radicals which become free agents causing biochemical havoc leading to cardiovascular and cerebrovascular disease such as clogging of the arteries, heart attack, stroke and dementia caused by insufficient blood supply to the brain (ischemic dementia). Free radicals are also known to cause inflammatory conditions and tissue damage, so antioxidants will act as protection against these.

It is thought that the unexpected effect of resveratrol in at least delaying the onset of Alzheimers disease is due to its reduction of the inflammation associated with the build up of amyloid plaques which cause the disease in the brain. Researchers have found that resveratrol makes human neural cells grow extensions enabling them to connect to neighbouring nerve cells. This may help to explain why wine drinkers have less of the neuro-degenerative diseases such as Alzheimer's disease (commonest form of dementia) and Parkinson's disease, as the resveratrol in the wine may help the nerve cells in the brain continue to grow and connect. In neurodegenerative diseases, these connections break down. It should be remembered that heavy alcohol consumption severely damages nerve cells leading to Wernicke's encephalopathy, Korsakoff's syndrome, peripheral neuropathy and other forms of nerve degeneration.

Resveratrol is processed by the enzyme CYP1B1, which is found in a variety of different tumours. This converts resveratrol into piceatannol, a closely related phytoestrogen with known anti-cancer activity. Previous research has shown that this process is restricted to the tumour itself, limiting the toxicity to the cancer cells and serving to selectively destroy them.

Scientists previously believed that CYPIBI was a cause of cancer because it is only found in tumours and not in healthy tissue. Researchers now think the enzyme is there to fight cancer and research continues as to how the enzyme and resveratrol work.

Corder and Crozier's research sheds doubt on the validity of resveratrol as the most important antioxidant, believing its quantities in red wine too insignificant to be valid. They believe procyanidins are more beneficial.

Important facts:

Common Antioxidants in beverages

Cider:	Quercetin
	Hydroxycinnamic acids
Beer:	Ferulic acid
	Catechin
	Epicatechin
	Xanthohumol
Wine:	Gallic acid
	Tannic acid
	Morin
	Quercetin
	Resveratrol
	Rutin
	Saponons
	Pterostilbene

Antioxidant activity in unfermented grape juice is lower than in the finished wine - antioxidant activity increases during fermentation and maturation. Antioxidant levels will depend on the processing, filtering for example, as well as on the variety, vintage, altitude and soil. Original research in Australia by Professor Geoff Skurray at The University of Western Sydney has shown that different wine filtration techniques during wine making may influence the amount of resveratrol left in the wine after filtration. Various fining agents commonly used by oenologists were tested. Polycar removed 92% of resveratrol. Casein, egg white and alginate also removed some resveratrol whilst gelatin had a variable but relatively little effect. So winemaking techniques, as well as grape variety (red wines contain more resveratrol than white) and growing season (summer rain years produce more resveratrol) play a role as to how much resveratrol there is in a wine. Similar research from Caroline Walker from Brewing Research international on Ciders and beers, has shown that the antioxidant activity in cider can vary from 2,500 to 10, depending on the producer.

Bioavailablity - does size matter?

The ease with which we can absorb any compound is called the bioavailability and this needs to be measured for each food and beverage individually to get an accurate picture of how good a source of antioxidants it is. It has been established that the consumption of two 100ml glasses of red wine a day may increase the phenolic content of the average diet by 40%, but only a weak correlation exists between polyphenolic content and antioxidant activity.

Ferulic acid, in contrast is highly absorbable. Although it has not been completely established, it would be expected that the larger bulky antioxidants are likely to stay in the gut rather than to get absorbed.

How and where are these molecules absorbed into the bloodstream?

A group in Italy has shown that antioxidants are transported directly through the stomach wall, which has cells in it containing a transport protein called Bilitranslocase. This molecule is also used by the body to get the waste product bilirubin out of the bloodstream into the liver, where it is metabolised for excretion: it is the product of the decay (natural) of red bloodcells. Bilirubin causes neonatal jaundice, and is responsible for the yellowish colour around bruises.

Bilitranslocase also interacts with anthocyanins, and transport them first into the bloodstream directly from the stomach, and then even into the liver and into brain tissue. While the amount absorbed is small, it gets to the named organs very rapidly. Furthermore, research suggests that once absorbed, antioxidants are often metabolised into other forms — forms which may have different biological activity. For example, much of the resveratrol is modified in the liver by coupling to glucuronic acid. Therefore establishing the absorption and further metabolism of antioxidants is a key factor in establishing their biological effects. We have also learnt that ethanol has a

Antioxidant activities of selected foods and beverages from Paganga et al (1999) *BRI/IFR project data source

	Portion size	Antioxidant activity
Apple (peeled)	100g	640
Tomato	100g	160
Aubergine	100g	490
Onion	100g	580
Red wine (Rioja-Bordeaux)	150ml	2100-3400
White wine	150ml	220
Black Tea (0.25%)	150ml	1400
Green Tea (0.25%)	150ml	1350
Cider*	250ml	100-2595
Apple juice (long life)	150ml	140
Orange juice	150ml	400
Blackcurrant juice	150ml	800

Furthermore, research suggests that once absorbed, antioxidants are often metabolised into other forms — forms which may have different biological activity. For example, much of the resveratrol is modified in the liver by coupling to glucuronic acid. Therefore establishing the absorption and further metabolism of antioxidants is a key factor in establishing their biological effects. We have also learnt that ethanol has a pro-oxidative effect on plasma lipids.

Hence the usefulness or bioavailability of the antioxidants available in alcoholic beverages is not yet fully established. However the importance of antioxidants themselves in vascodilation, fighting cancer and dementia are established and further research as to absorption by the human body is needed.

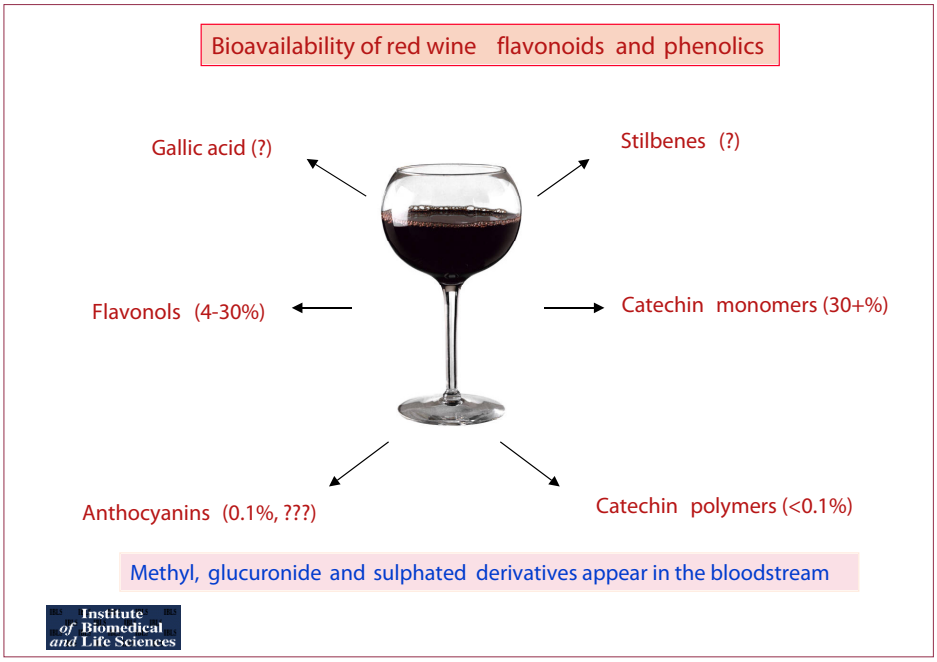
AIM Council comments on antioxidants

Harvey Finkel MD of the Boston University School of Medicine:

"At or near the top of causes of death and disability are diseases of the heart and blood vessels, cancer, and degenerative disorders. Free radicals and oxidation figure heavily in the causation and aggravation of these ills. Free radicals, are highly reactive compounds produced normally as the body uses oxygen. Smoking, radiation, and certain chemicals enhance their production, thus straining, sometimes overwhelming, the body's natural enzyme-mediated antioxidant defense system. This is why there is so much interest in importing additional antioxidants, those derived from food and drink. Look at a partial list of diseases suspected of being able to be relieved by antioxidants: heart attack, stroke, other complications of blood-vessel disease, cancer, Alzheimer's disease and other dementias and degenerative disorders, immune dysfunction, cataract, macular degeneration. Aging itself may be retarded by antioxidants. Precise formulas for each of us are not yet possible - we have much to learn. Antioxidants may not always be entirely benign".

Dr Erik Skovenborg of the Scandinavian Medical Alcohol Board:

"The question of bioavailability is a crucial question: if you drink a bottle of full-bodied red wine you consume about 2 grams of red wine polyphenols (RWP); what part of these healthy compounds is absorbed during the process of digestion to become available to target tissues like the endothelial cells of blood vessels or the nerve tissue of the brain? Professor Castanas has good news to wine drinkers: alcohol protects the RWP, so a glass of Cabernet Sauvignon is a good vehicle for polyphenols. For those who want a steak on the plate to go with their Cabernet here is more good news: proteins have a dual action protecting the RWP from oxidation and increasing the bioavailability of the healthy compounds. That added bonus leads directly to Elias Castanas' favourite advice concerning a sufficient daily intake of polyphenols: eat a normal meal with a variety of foods like fruit, vegetables, legumes, olive oil, bread and fish accompanied by moderate consumption of wine".



Alan Crozier professor of plant biochemistry and human nutrition, University of Glasgow:

'I think that resveratrol is not an important component in the protective effects of red wine. The levels in red wine are low and to get the effects that have been observed in animals, humans would have to consume more that 1000 litres of red wine daily ! The paper co- authored by Roger Corder and myself in Nature in November, strongly implicates procyanidins in wines' protective effect'.

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