



# dr paul clayton's

## Health Newsletter

Autumn 2008

Vitamin D  
Eyes – AMD  
Flavonoids

While in the last newsletter we were talking of summer holidays in the Mediterranean, here we are, I'm afraid, looking forward to the cold and flu season. So here is the very latest on nutritional strategies - for the full story on Winter Defence, check out my website [www.winterdefence.com](http://www.winterdefence.com).

Plus we also report on more research on flavonoids (Vitamin P), updating our Spring 2007 newsletter.

### Vitamin D - a very hot topic



Vitamin D has now been shown to be essential for AMP production (Schauber et al '07), to enhance the microbe-killing activity of macrophages and neutrophils (Schauber et al '07), and assist the formation of Natural Killer Cells (Yu & Cantorna '08).

All this means that if you are depleted in vitamin D – as most Britons are for most of the year – your innate immune system is well below par. And as autumn blends into winter and then into early spring, our falling D levels make us ever more prone to infections.

This has finally been convincingly identified as the reason why colds and flu are more prevalent in winter months (Cannell et al '08). As vitamin D depletion causes immune impairment, and vitamin D restores it (Aloia & Ng '07), supplements of the summer vitamin should help to keep you free from winter infections.

For best results it should be combined with **1-3, 1-6 beta glucans** and **selenium** (Beck et al '95, '03), which work in different but complementary ways. This pharmaco-nutritional combination should keep you healthy through the winter.

As the cancer industry has successfully scared us all to death about venturing into the sun, thereby preventing us from making enough of our own vitamin D, and as the bulk of the UK population is depleted in selenium (Rayman '97), this constitutes yet another powerful argument for supplementation. Despite all the guff from the traditional nutritionists about getting all you need from a 'well-balanced diet'.

Vitamin D is becoming an ever hotter topic in nutritional research.

Once known as the bone vitamin, recent research has revealed that its principal functions are, in fact, related to the immune system. The importance of vitamin D in reducing the risk of autoimmune disease was discussed in a previous newsletter. This kind of disease involves the most complex part of the immune system, known as the acquired immune system.

The most basic – and most important – part of the immune system is the **innate immune system**. This in turn consists of three elements: (1) barriers such as the skin, (2) broad-spectrum antibiotic compounds such as the Anti-Microbial Proteins (AMPs) and (3) an array of immune cells. These include macrophages and neutrophils, which kill bacteria, and Natural Killer Cells, which kill virally infected cells.

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## Flavonoids - to P or not to P?

The flavonoids were known as vitamin P until pharmaceutically-minded medics decided that nutrition was unimportant and flavonoids were irrelevant to health. That, of course, is changing fast; flavonoids are emerging as one of the most important phytonutrient categories of all. But although high flavonoid intake is strongly related to better health prospects, there is a real argument as to how they might be working in the body.

A recent review concluded that while flavonoids are effective antioxidants *in vitro*, they are not effective antioxidants in the body (Lotito & Frei '06). The authors cited research which indicates that only about five per cent of ingested flavonoids are actually absorbed by the body, and most of what does get absorbed into the blood stream is rapidly metabolised and excreted. According to Professor Frei, director of the Linus Pauling Institute at Oregon State University, "The body sees flavonoids as foreign compounds and modifies them for rapid excretion in the urine and bile. It seems highly unlikely that flavonoids make a significant contribution to antioxidant protection of plasma and other extracellular fluids *in vivo*."

The authors concluded that the flavonoids exerted many of their effects by up-regulating the body's detoxifying enzymes, thereby improving the body's ability to detoxify and excrete carcinogens. It is clear, however, that the flavonoids and/or their metabolites have many other effects in the body, including anti-inflammatory, analgesic, and gene regulating effects.

Flavonoid extracts of the spices ginger and turmeric, for



**TURMERIC**

example, are widely used to treat the symptoms of arthritis. They are reported to be approximately as effective as standard anti-inflammatory drugs (Satoskar et al '86, Srivastava & Mustafa '92), and work almost as rapidly (Strand '07); which



**GINGER**

strongly implies that some flavonoids, at least, are taken up by the body very effectively.

Other flavonoids shown to be clinically effective include pycnogenol, a blend of flavonoids derived from pine bark; and the anthocyanins, derived from berry fruits.

Pharmacokinetic studies which repeatedly fail to find significant levels of flavonoids in the bloodstream may, therefore, be looking in the wrong place. This could be because most flavonoids have a very high affinity for connective tissues – a fact you can easily check for yourself at this time of year. Just go picking blackberries and you soon find that the blackberry juice stains your hands purple. That staining is the coloured berry flavonoids sticking to the connective tissue in your skin.



Something similar probably happens when you eat flavonoids. Once absorbed into the blood stream, their high affinity with connective tissue ensures that they rapidly leave the blood and enter the blood vessel linings; where they may be transformed into active metabolites (Adlercreutz '97).

Lotito and Frei concede it is possible that flavonoids "... may accumulate in tissues where they might exert local antioxidant effects, or that very low concentrations of flavonoids may modulate cell signalling, gene regulation, angiogenesis, and other biological processes by non-antioxidant mechanisms, which may explain the purported health benefits of flavonoids."

In fact, Lotito and Frei have taken a remarkably conservative line. There is plenty of evidence that various flavonoids are indeed absorbed, and rapidly partition into the tissues where they play so many critical roles in maintaining our health.

One of the great experts, Professor Herman Adlercreutz at the University of Helsinki, specialises in isoflavones and flavolignans which are related to the flavonoids. Professor Adlercreutz has published numerous papers demonstrating the importance of these compounds, and the fact that they tend to be taken up into the tissues (Rannikko et al '06).

Although much work remains to be done, it seems very probable that different flavonoids target specific tissues, as the folk medicine has always implied. The link between flavonoid intake (from chocolate, soy and tea), improved vascular function and a reduced risk of coronary artery disease is already very persuasive (ie Hooper et al '08).

Recently, the cancer story has been gaining ground as well. For example ...

## Flavonoids and cancer

A new study at the University of California in Los Angeles has found that the risk of **lung cancer** amongst smokers may be decreased by as much as 50 per cent by an increased intake of certain flavonoids (Cui et al '08). Increasing intakes of epicatechin, catechins, kaempferol and quercetin, four related compounds found in tea, apples and onions, were associated with increased reduction of risk.

Specifically, a 10mg per day increase in **epicatechin** intake

reduced the risk by 36 per cent, a 4mg increase in **catechin** intake

reduced the risk by 51 per cent, a 9mg increase in **quercetin** intake

reduced the risk by 35 per cent, and a 2mg increase in **kaempferol** intake reduced the risk by 32 per cent.

The authors pointed out that their study was not definitive, but could not resist talking about the flavonoids' anti-cancer mechanisms such as their ability to persuade cancer cells to commit suicide.

Meanwhile, over at the National Cancer Institute in Maryland, another research team almost simultaneously published a paper on flavonoids and **colorectal cancer**. In this paper, increased intake of flavonols (a sub-set of flavonoids) was linked to a 76% reduction in the risk of recurrence of advanced tumours, in a group of people already diagnosed with polyps (Bobe et al '08).

**Flavonols** occur in **tea, onions, beans and apples**, but



perhaps the best source of these compounds is **cocoa**. Regular readers may remember that the Kuna Islanders, who consume huge quantities of cocoa flavonols, have rates of heart disease and cancer about 90% lower than ours (Bayard et al '07).

In Potsdam, Germany, a third group found that a diet rich in flavonols was linked to a 25% reduction in the risk of **pancreatic cancer**; with a 60% reduction in smokers, who are at much higher risk in the first place (Nöthlings et al '07).

Once again, the key 'protective' compounds were **kaempferol** and **quercetin**; together with **myricetin**, a related compound found in red onions and berries.

An alliance at the University of North Carolina and 7 other top-notch medical centres published findings indicating that in

post-menopausal women consuming higher levels of flavonoids, **breast cancer** survival might be improved, with an approximately 40% reduction in breast cancer and all-cause mortality (Fink et al '07).

And in Italy, a research group based at the well-known Mario Negri Institute in Milan found that the risk of **kidney cancer** was also reduced by higher flavonoid intake (Bosetti et al '07). In



this study the risk was reduced by around 30% in subjects consuming high levels of flavones and, once again, flavonols appeared to be most protective.

In short, a mounting body of science including epidemiological, laboratory-based and randomised clinical trials, continues to report the cancer-fighting potential of a number of different flavonoids. And with cancer in particular, a few grams of prevention are worth many kilos of cure.

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## Eyes right

When skin is exposed to sunlight, it tans – except for Celtic skin, of course, which tends to burn. Tanning is a defence mechanism, whereby increased levels of the pigment melanin in the skin protect it against radiation damage. A very dark skin can have an in-built SPF of up to 8 or 9. The eyes, for obvious reasons, cannot protect themselves in this way, and this is one reason why many people eventually develop a form of retinal damage called macular degeneration: a type of blindness which affects about 30 million people world-wide.



There is a large and rapidly developing body of evidence that two compounds in the diet called **lutein** and **zeaxanthin**, members of a group of phytonutrients known as xanthophylls, play a critical role in protecting the retina (ie AREDS '07, Stringham & Hammond '08). They are present in foods such as **spinach**, **squash**, **kale** and **avocado**, and in the body they are found in the macula densa, a pigmented layer of tissue that lines the back of the eye. They are believed to reduce the risk of AMD by absorbing frequencies of sunlight that could otherwise damage the macula, thus preventing free radicals from damaging the delicate rod and cone cells in the retina.

There are many studies that support this hypothesis, both in animal models and in humans; but until very recently, the story was incomplete. It was known that xanthophylls are absorbed in the small intestine, pass into the blood and are taken up into LDL cholesterol – the so-called 'bad cholesterol' which is actually a vital transport system. But nobody understood how these compounds managed to travel into the eye.

Now the final link in the chain has been revealed by a American – Belgian collaboration (During et al '08). Working with human pigmented retinal epithelial cells in vitro, the scientists found that lutein and zeaxanthin are transported into the cells by a transport protein called SR-B1, or scavenger receptor class B,

type 1. This is a very specialised protein, which – by no coincidence – is also involved in the uptake of lutein and zeaxanthin from the gut.

The story is now nearly complete. Eating a poor diet, or having a genetic mutation which damages SR-B1, increases the risk of macular degeneration. Conversely, eating a diet rich in fruits and vegetables and therefore containing higher amounts of xanthophylls results in higher levels of these compounds arriving in the retina; and a greatly reduced risk of macular degeneration. Following the 5-portions-a-day mantra appears to reduce the risk by about a third (AREDS '07), but if you want real protection, you probably need to eat around 10 portions of fruit and vegetables a day (Clayton & Rowbotham '08a, b, c).

Alternatively, you could take a supplement. In the USA, the Food and Drug Agency has declared lutein and zeaxanthin to be GRAS (Generally Regarded As Safe), thereby giving these compounds the green light for use in supplements or as food ingredients.

I would not recommend taking high doses of lutein and/or zeaxanthin on their own; as with beta carotene, that could be counter-productive (Kalariya et al '08). As two elements in a broad-spectrum pharmaco-nutritional support programme, however, they are essential; even although RNI values have not yet been established.



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