



Dr Paul Clayton's Health Newsletter

Nutrients on the brain

The latest nutrient craze is a supposedly new vitamin called **pyrroloquinoline quinone**. As the name of this compound doesn't exactly roll off the tongue, we are fortunate indeed that it is routinely abbreviated to **PQQ**. PQQ is being boosted on a number of websites, where companies are selling it (under related names such as BioPQQ) as not only a new B vitamin but also the key to brain health. It is claimed to be an antioxidant (whatever that is), a booster of nerve growth factor and a mitochondrial support, and as such the answer to brain fog, brain ageing and even brain disease.

Is it really all these things? Let us look at these claims in more detail.

? PQQ is a new vitamin ? Well, in 2003 a Japanese research group (Kasahara et al '03) published an interesting paper in the august journal *Nature* in which they made a case that PQQ might indeed be a vitamin, citing evidence based on some rather esoteric molecular modelling. In 2005, however, that same journal published a paper by a US team (Felton & Anthony '05) which pointed out key mistakes in the earlier work. Bottom line – PQQ is a fascinating molecule with a number of valuable functions in the body, but it is probably not a vitamin.

? PQQ acts as a nerve growth factor (NGF) ? Maybe. There are some ex vivo data showing that PQQ can help rat nerves to grow in silicon (Liu et al '05), and increases NGF synthesis (Zhang et al '12) but doubt remains as to whether PQQ supplements can increase or mimic nerve growth factor in human brains. If it does so, this could be a useful anti-ageing tool. I tend to believe that PQQ does indeed have this effect but the jury is still out.

? PQQ triggers growth of new mitochondria ? a process sometimes termed mitochondrial neogenesis. Ahah! Here is a potentially important claim, as mitochondrial ageing is a deep and strategic component of ageing and

anything that enhances or renews mitochondrial function (and therefore the cells' ability to produce usable energy) would have many therapeutic effects. And here the case is clearer; the balance of the available evidence suggests that PQQ can both protect mitochondria against oxidative and other stresses (Xu et al '14) and, under favourable circumstances, trigger the growth of new mitochondria (Chowanidisai et al '10). Moreover, broadly analogous effects have been shown in human subjects (Harris et al '13), where PQQ supplements of 30 to 40 mg resulted in improved mitochondrial function and related anti-inflammatory benefits.

So, should we all start adding PQQ to our already onerous list of nutrients? Not so fast ...

There are many antioxidant compounds in our foods and in our bodies, and quite a few that have the ability to get inside the mitochondria and protect them from oxidative stress. These include the well known melatonin (Guo et al '14) and Q10 (ie Noh et al '13), the latter compound being essential to mitochondrial function.

But there are many other nutrients that both protect mitochondria and trigger mitochondrial neogenesis, including dozens and perhaps hundreds of **polyphenols** (Laurent et al '12) ranging from the **resveratrol** in red wine (Davinelli et al '13, Kim et al '14) to the **equol** derived from soy (Davinelli et al '13), the more widely occurring **catechins** in tea and cocoa (Moreno-Ulloa et al '14), the ubiquitous **quercetin** (Davis et al '09), and the truly fascinating **olive polyphenols** (Zhu et al '10).

The polyphenols have multiple beneficial effects in the body which are broadly tissue protective and anti-inflammatory, but their regulatory status – despite a large body of evidence indicating that the polyphenols are, collectively, a vitamin – remains unclear. This regulatory omission is causing us enormous harm.



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The Paul Clayton Health Newsletter

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- All references on the back page
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"In populations which consumer higher amounts of anti-inflammatory polyphenols and omega 3s, levels of inflammatory diseases are around 10% of those in our 'civilised' societies."



Quercetin in apples



Catechins in green tea



Olive polyphenols

"Metabolism was 'designed' by evolution so that life can continue even if one nutrient is temporarily unavailable, as others can fill in."

PQQ or Polyphenols? contd

Just as a reminder, polyphenols are a large group of structurally related compounds that occur widely in plants, and in all but the most processed plant-derived foods. Unfortunately it is the latter, highly processed food that have been thrust down our collective throats by an out-of-control food industry, working with regulatory regimes (EU-EFSA and USA-FDA) which have been captured and corrupted by the industries they nominally oversee (Light et al '13). These regulators have allowed the creation of a food universe which is grossly unhealthy.

Our food universe is not only depleted in polyphenols but also in omega 3 fatty acids and 1-3, 1-6 beta glucans. This has left us extraordinarily vulnerable to chronic inflammation, as shown by the current multiple pandemics of degenerative disease. In populations which consume far higher amounts of the anti-inflammatory polyphenols and/or omega 3s, inflammatory diseases such as heart disease, diabetes, stroke and cancer are around 10% of the levels in 'civilised' society (ie Bang et al '80, Bayard et al '07).

We urgently need to put this right. There are honest regulators and even (possibly) a few honest lawmakers, but they are stuck in the past. Their idea of nutrition is still influenced by early work on vitamins which set in stone the idea that specific nutrients have a key and unique role in the body, and are the only compounds that can do this. But this is far from the truth.

Many nutrients have multiple functions in the body, and many functions can be modulated by multiple nutrients. Metabolism is not linear but stochastic; there is an overwhelming complexity and a huge degree of redundancy. It was 'designed' thus by evolution so that life can continue even if one nutrient or handful of nutrients is temporarily unavailable, because others can fill in to a greater or lesser extent, at least for periods of time. We still have unique dependencies (a handful of vitamins, essential amino acids and essential fatty acids), but these represent a very small proportion indeed of the many tens of thousands of compounds that flow, merge together and separate in our bodies to enable the enormous complexity and dynamism of life.

Let's loop back to where we started. Take PQQ if you like, but you will be better off, in my opinion, consuming large amounts and numbers of different polyphenols in foods and/or supplements.

Polyphenols to treat depression

Curcumin, the polyphenol derived from turmeric, is already known to have anti-inflammatory effects and to be cardio-, neuro- and chemo-protective; in the last 8 years, over 7000 studies have been completed. Now turmeric appears to be an anti-depressant too.

Various teams of scientists have shown that curcumin exerts anti-depressant activity in animal models of depression (ie Zhang et al '14, Jiang et al '14, Zhao et al '14). And within the last year, three reasonably powerful clinical trials found that curcumin was more effective than placebo (Lopresti et al '14), as effective as Prozac (Sanmukhani et al '14) and it increased the effect of anti-depressant drugs (Panahi et al '14). Notably, when examining the effects of curcumin in people with atypical depression, which is generally more difficult to treat, curcumin had even greater antidepressant and anti-anxiety efficacy (Lopresti et al '14). Moreover, curcumin treatment was free of adverse side-effects.

Current antidepressant drugs have limited efficacy in controlling the symptoms of major depressive disorder, and are associated with multiple and occasionally serious adverse events particularly when used long-term. Finding a natural dietary substance that is as effective as Prozac, but does not cause side effects (such as 'going postal') is a real breakthrough, especially as depressive illness has increased so dramatically over the last few decades.

How does curcumin alleviate depression?

This is a moot question, particularly when nobody is even really sure how the anti-depressant drugs work, but a consensus is beginning to form. And it is a complex one ...

There is evidence that three distinct but inter-related metabolic / physiological issues underlie depressive illness. These are chronic inflammation (Han & Yu '14, Abelaira et al '14, Popo-Wagner et al '14), disturbed communication between the thalamus, hypothalamus and pituitary (Zajkowska et al '14), and disruption of endocannabinoid chemistry (Crowe et al '14).

Curcumin and many other polyphenols have potent anti-inflammatory effects (too many references to cite here!) and anti-stress effects (ie Fisher et al '14, Poirier et al '14) which would reduce or prevent the in-brain communication problems. The polyphenols also exert anti-oxidant effects which may well impact on endocannabinoid chemistry (ie Nunn et al '10), and

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so they appear to protect against all three of the problems thought to drive depressive illness.

Which brings us to a grand, unifying theory.

Changes in our diet (thanks again to the multinational food companies) have reduced our intake of omega 3 fatty acids and increased our intake of omega 6. This has dramatically increased the 6:3 ratio in what we eat—and therefore inside our skulls—from about 2:1 in 1900 to 20:1 or even higher today.

Our intake of polyphenols has also fallen considerably, and this unfortunate dietary combination of reduced omega 3s and reduced polyphenols has left most of us in a semi-permanent state of chronic inflammation. Our endocannabinoid chemistry has greatly changed, as these compounds are derived from the type of fats in our diet. And our exposure to stress is arguably as high today as it has ever been. To make matters worse, the prevalence of Type B malnutrition (micronutrient depletion) may well have altered our brain's ability to make neurotransmitters.

From this perspective, it is not so surprising that depressive illness has become so prevalent. It may also explain the increase in marijuana use, now so widespread as to be forcing decriminalisation. If endocannabinoid chemistry is in a bad way, self-medication with phytocannabinoids could actually make sense (as well as being, I'm told, occasionally amusing).

For those who do not wish to experiment with marijuana there is PEA. PEA – or to give it its full name palmitoyl ethanolamide – is an endocannabinoid which is available as a supplement and used as an anti-inflammatory analgesic. PEA has also been found to have anti-depressant activity (Yu et al '11), but it does not get you high. Better take PEA and flavonoids, a combination which shows significant anti-depressant effects even at very low doses (Cupri et al '14).

Better yet to eat nutrient-dense foods and get a good omega 6:3 ratio in your diet. In a well-nourished population, I believe that both depressive illness and cannabis usage would be greatly reduced.



Turmeric root and powder

Unhappy meals – addictive junk foods

It baffles me why anyone would want to eat at any of the US-type fast food outlets.

I tried a burger from a leading chain recently, out of a mixture of curiosity and extreme hunger, and found it almost completely tasteless apart from the salt. There was a lot of salt, a good deal of grease, a cheap and nasty white bun (which is turned in the gut into sugar), and a small slab of cooked pink slime – quite revolting, really.



I didn't stay for long but I couldn't help noticing that the outlet had a very particular clientele, of a type I have seen in burger and related joints in many countries. Overweight, bad complexions, generally unhappy, poor impulse control (very easily distracted), bad teeth. This is of course a huge generalisation; there are many who do not fit that bill – but it is prevalent.

It is hardly surprising that such appalling food would produce this kind of customer, and nor is it surprising that the developed nations are experiencing such a burden of bad health.

This kind of junk diet is deeply pathological. It combines electrolytes in a ration that predisposes to hypertension (high blood pressure), with a lack of fibre increasing risk of bowel and many other diseases, an excess of sugars which contributes to diabetes, heart disease and multiple other conditions, an excess of AGEs and ALEs (pro-inflammatory toxins produced when foods are cooked at high temperatures), which are linked to Alzheimer's, heart disease and cancer, a lack of 1-3, 1-6 beta glucans leading to increased risk of allergy, and a lack of the anti-inflammatory omega 3s and polyphenols which causes chronic inflammation and many degenerative diseases.

So why do folk keep eating this junk? For one thing, it is cheap.

“Food manufacturers know exactly how to hit what they call the ‘bliss point’, combining salt, sugars, fats and texturisers with clever marketing strategies to make foods which, scientists increasingly believe, are psychologically and physically addictive.”

NutriShield contains polyphenols (green tea, curcumin, grapeseed, bilberry) and **omega 3**.
nutrishield.com

ImmunoShield contains 1,3 1,6 beta glucans.
immunoshield.com

Why do folk keep eating this junk? For one thing, it's cheap!

The Dr Paul Clayton Health Newsletter describes developments in the field of pharmaco-nutrition, where nature and science are combined to offer non-drug solutions to degenerative disease.

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Unhappy meals—addictive junk foods contd

The food industry has been captured by a handful of agro-business companies (Google them!) who grow a very limited number of staple foods such as corn, soy and wheat; and by a slightly larger number of multinational but predominantly American food manufacturers. These corporate players form an oligopoly large and wealthy enough to rent all the regulators and politicians they need, and get them to do more or less what they like. They use this kind of leverage to kill off competitors, and force through government subsidies for themselves; enabling them to produce cheap foods and spend billions advertising their shoddy products.

Cooked and processed burgers, fries and shakes are significantly cheaper than fresh fruits and vegetables, which are not subsidised. And the food manufacturers know exactly how to hit what they call the 'bliss point', combining salt, sugars, fats and texturisers with clever marketing strategies to make foods which, scientists increasingly believe, are *psychologically addictive* (refs 1-6).

A new study (7), in which a junk food diet led not only to weight gain but abnormal and degraded appetite and food selection, adds considerable weight (sorry) to the argument. This study also indicated that there may be an element of *physiological addiction*, which would explain why excessive consumption of junk foods high in sugar, salt and fat can change behaviour, weaken self-control and lead to overeating and obesity.

In this important experiment, rats fed a cafeteria diet containing high-fat foods such as cookies, dumplings and cake rapidly lost their taste for novel foods (a strategy which favours a balanced diet) and became indifferent in their food choices. In short, a junk food diet was self-sustaining, with poor food choices leading to more of the same poor choices.

The paper suggested that consuming a junk diet caused lasting changes in the reward circuit parts of the rats' brain such as the orbito-frontal cortex, an area responsible for decision-making. This has definite implications for humans who are probably equally unable to limit their intake of certain kinds of foods, because the brain's reward circuitry is similar in all mammals. "As the global obesity epidemic intensifies, advertisements may have a greater effect on people who are overweight and make snacks like chocolate bars harder to resist," said the paper's lead author.

The case against the food industry looks stronger by the day. If it can be shown that the food manufacturers are aware of the addictive nature of their highly processed products, they will deserve the truly massive lawsuits which will soon be landing in their in-trays. World Health Organisation Director Margaret Chan is leading the way, and has threatened food companies with on-pack health warnings unless they start to shape up.

"Cooked processed burgers, fries and shakes are significantly cheaper than fresh fruits & vegetables which are not subsidised."

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