

We are what we eat. Or are we?

Early communication of basic research

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INTRODUCTION

As far back as Ayurveda (an ancient Indian system of complementary and alternative medicine, dated to 2000 BC¹), food has been linked to the health of its eater. However, this concept has only recently become valid in mainstream medicine, with more research endorsing it and governmental policies implementing it. For example, in the 1980s, a Japanese national research project started to scientifically prove the health-benefits of functional foods (or 'good' foods) in order to improve the nation's health². Devcich et al cite the definition of functional foods as "foods that are part of a normal diet which have been fortified or enriched to provide additional health-promoting benefits in conjunction with normal nutritive properties"³. These are foods that protect against pathological mechanisms causing disease and promote physiological functions. Some examples of functional foods include fruit, vegetables, fish and nuts.

One of the disease-promoting mechanisms that functional foods are thought to prevent, or even reverse, is Oxidative Stress (OS). OS is a state of imbalance in which an organ's endogenous antioxidant mechanisms fail to protect it against the accumulating reactive oxygen and nitrogen species. These reactive species result from metabolic interactions taking place in the organ and can have deleterious effects on the function and survivability of cells. Reactive oxygen and nitrogen species can cause DNA and RNA damage, lipid peroxidation, and the oxidation of proteins and amino acids, all of which can result in cell death and degeneration^{4,5}. The central nervous system (CNS) is particularly susceptible to OS. This is due to factors such as lipofuscin accumulation, increased lipid peroxidation, reduced active redox iron, changes in lipid membranes, and aging⁶. It is, therefore, clear why research has associated OS with the development of neurodegenerative diseases such as Parkinson disease (PD)⁴.

PD is the second most common neurodegenerative disorder after Alzheimer's disease⁷. Named after James Parkinson in 1817, it is characterised by the loss of dopaminergic neurons of the substantia nigra pars compacta region of the brain. It leads to motor impairments (bradykinesia, tremor and rigidity), as well as non-motor manifestations (such as depression, sleep disorders and autonomic disturbances). Since PD has long been linked to food, it serves as a good model on which to base this article.

Foods causing PD?

In the late 1980s, a hypothesis linking a toxin present in tomatoes with PD was generated and published in the medical literature⁸. As arbitrary as it

may sound, it was actually based on a sophisticated use of scientific critical thinking and epidemiological methodology. It seemed to the physicians of those times that PD affected people in rural areas more often than people in urban areas; and that the incidence of PD increased with age⁸. Moreover, we see that tomatoes, after being confined to Mexico, Italy and some other areas of Europe since 1544, had only been introduced to North America and Western Europe in the early 1800s (around James Parkinson's time, when he first wrote about this condition in London, England)⁸. Furthermore, the slow accumulation of the toxin from tomato consumption could account for the higher incidence of PD in rural people, assuming they have a higher consumption of fruit and vegetables; and for the increased incidence of PD with age⁸. This hypothesis was never proven and tomatoes are no longer linked with the causation of any disease.

Foods protecting against PD?

On the other hand, there is a growing body of evidence indicating that fruit (including tomatoes which are fruit!) and vegetables do offer some form of protection against many diseases. These include various degenerative diseases, such as cardiovascular diseases, some cancers and neurodegenerative disorders⁹. Fruits and vegetables contain compounds known as phytochemicals which are thought to offer the health-promoting effects. The exact mechanism by which these chemicals exert their effects is unknown. However, some evidence now supports the idea that the antioxidant properties of these compounds may exert their disease-preventative effects through reducing the OS expressed by cells such as by dopaminergic neurons in PD⁹.

The most widely studied group of phytochemicals is a sub-class known as anthocyanins. These are a group of secondary compounds that a plant produces. These are compounds that serve ecological functions to improve the plant's survivability⁶. They are responsible for the attractive red, purple and blue pigments seen in some fruit and vegetables, such as in berry fruits, eggplants and red cabbage. *In vivo* and *in vitro* studies have shown that anthocyanins are very potent antioxidants. A particularly anthocyanin-rich fruit is blackcurrants (Latin *Ribes nigrum*); they have been shown to be the second most active radical scavenger amongst nine other types of berries⁹. New Zealand is well-known for its production of high-quality blackcurrants¹⁰. The four main anthocyanins of blackcurrants are C3G, D3G, C3R and D3R⁹. These four anthocyanins and their metabolites are believed to be the chemicals that could potentially provide neuroprotection to patients with PD.

The use of blackcurrants as a neuroprotective agent in patients with PD has been described in the medical literature with some interest and promise. Blackcurrant anthocyanins have been shown to provide antioxidant effects in *in vivo* and *in vitro* animal studies^{11,12}. For example, when rats were fed a diet of blueberries (another anthocyanin-rich fruit), anthocyanins were found to localise in different regions in the brain and the rats showed improvement in behaviour and memory¹¹. Studies on human subjects, however, have been less conclusive on the effects of anthocyanins. Even though blackcurrant anthocyanins are rapidly absorbed from the stomach and small intestine, their clearance in the urine appears to be rapid too. One study has found that after six hours, very little anthocyanins remains

in the plasma¹³. Moreover, another study showed that the proportion of anthocyanins absorbed was very low when compared to intake level, indicating the blackcurrant anthocyanins undergo extensive metabolism in the body¹⁴. However, the metabolites were found to preserve the antioxidant activity of anthocyanins¹⁴. Lastly, in order to deliver these antioxidants to the brain, the blood-brain barrier (BBB), a unique endothelial barrier protecting the CNS and regulating molecular transportation across to the neural structures, needs to be traversed. To date, it has been shown that anthocyanins have been present only in brains of animal models (rats and pigs)¹⁵. The question as to whether anthocyanins can penetrate the human BBB and localise in the brain still needs to be investigated.

CONCLUSION

The shift in the 'food paradigm' from being merely linked to a person's health (whether good or bad!), to preventing human-diseases is very interesting and is showing some promise. Although research on this topic is still in its early days, there is potential for 'food-drugs' to offer some health-promoting benefits. Indeed, this arena of therapy may well unify orthodox medicine and complementary and alternative medicine, and turn pharmaceutical companies to pharmaceutical ones!



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REFERENCES

1. Medicine Net [internet].
Ayurveda.
June 2004. Available from: <http://www.medterms.com/script/main/art.asp?articlekey=10787>
2. Arai S.
Global view on functional foods: Asian perspectives.
Br J Nutr. 2002 Nov;88 Suppl 2:S139-43.
3. Devcich DA, Pedersen IK, Petrie KJ.
You eat what you are: modern health worries and the acceptance of natural and synthetic additives in functional foods.
Appetite. 2007 May;48(3):333-7.
4. McGhie T, Barnett L, Matuschek M, Vather R, Martin H, Alspach P, Kruger M.
Berryfruit Cognitive Study.
[unpublished].
5. Shan X, Chang Y, Lin CL.
Messenger RNA oxidation is an early event preceding cell death and causes reduced protein expression.
FASEB J. 2007 Sep;21(11):2753-64.
6. Barbara Shukitt-Hale Rachel L, Galli, Vanessa Meterko, Amanda Carey, Donna F. Bielinski, Tony McGhie and James A. Joseph.
Dietary supplementation with fruit polyphenolics ameliorates age-related deficits in behavior and neuronal markers of inflammation and oxidative stress.
AGE. 2005 May;27(1):49-57.
7. Mehta P, Kifley A, Wang JJ, Rochtchina E, Mitchell P, Sue CM.
Population prevalence and incidence of Parkinson's disease in an Australian community.
Intern Med J. 2007 Dec;37(12):812-4.
8. Sage JL.
Tomatoes and Parkinson's disease.
Med Hypotheses. 1989 Feb;28(2):75-9.
9. Kapasakalidis PG, Rastall RA, Gordon MH.
Extraction of polyphenols from processed black currant (*Ribes nigrum* L.) residues.
J Agric Food Chem. 2006 May 31;54(11):4016-21.
10. Just The Berries, Co. [internet].
Blackcurrants.
2007. Available from: <http://www.blackcurrants.co.nz/blackcurrants.php>
11. Andres-Lacueva C, Shukitt-Hale B, Galli RL, Jauregui O, Lamuela-Raventos RM, Joseph JA.
Anthocyanins in aged blueberry-fed rats are found centrally and may enhance memory.
Nutr Neurosci. 2005 Apr;8(2):111-20.
12. Walton MC, Lentle RG, Reynolds GW, Kruger MC, McGhie TK.
Anthocyanin absorption and antioxidant status in pigs.
J Agric Food Chem. 2006 Oct 4;54(20):7940-6.
13. Youdim KA, Shukitt-Hale B, MacKinnon S, Kalt W, Joseph JA.
Polyphenolics enhance red blood cell resistance to oxidative stress: in vitro and in vivo.
Biochim Biophys Acta. 2000 Sep 1;1523(1):117-22.
14. Xiong S, Melton LD, Eastal AJ, Siew D.
Stability and antioxidant activity of black currant anthocyanins in solution and encapsulated in glucon gel.
J Agric Food Chem. 2006 Aug 23;54(17):6201-8.
15. Kalt W, Blumberg JB, McDonald JE, Vinqvist-Tymchuk MR, Fillmore SA, Graf BA, et al.
Identification of anthocyanins in the liver, eye, and brain of blueberry-fed pigs.
J Agric Food Chem. 2008 Feb 13;56(3):705-12.