NEW INVESTIGATOR PAPER

'Superfoods' and the antioxidant fallacy: The impact of (poly)phenols on cardiovascular health

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'Let food be thy medicine and medicine be thy food' is attributed to Hippocrates and is still a pertinent message in today's society. The general population are fascinated by the impact of food on health and the media frequently report on the next dietary trend. The term 'superfood' is commonplace in modern day vocabulary. According to the Oxford English Dictionary it is used to describe 'food considered especially nutritious or otherwise beneficial to health and well-being'; arguably almost all foods could be defined in this way, making the term somewhat redundant. Nonetheless, berries, green tea and cocoa are commonly referenced as 'top superfoods' and one thing these foods have in common is high quantity of (poly)phenols; a class of secondary plant metabolites ubiquitous in the foods we eat suggested to reduce risk of many non-communicable diseases. (Poly)phenol classification with example foods is shown in Figure 1.

Evidence for cardio-protection

Interest in the association between (poly)phenols and cardio-protection stemmed partially from observation of the Kuna Indians. Kuna Indians inhabit islands off the coast of Panama but have much lower blood pressure and incidence of cardiovascular diseases than their Panamanian neighbours; one notable feature of their diets is their high intake of a cocoa drink high in (poly)phenols. (Poly)phenols have since been attributed to explaining the French Paradox; a phenomenon whereby the French have a low incidence of cardiovascular disease despite their high saturated fat intake. Epidemiological data for flavonoids (the most researched class), demonstrates reduction of cardiovascular disease risk¹. Many randomised controlled trials have attempted to prove causality between (poly)phenols and reduction in cardiovascular disease risk factors with evidence for improved vascular function²; however, the

trials are relatively small scale and short term. The results of the COSMOS trial, a 22,000 participant, 5-year intervention with cocoa flavanols focusing on cardiovascular events are due this year and are hotly anticipated.

Mechanism of action

(Poly)phenols in foods exhibit strong antioxidant capacity *in vitro*, for this reason it was long (and is still frequently) reported that the benefits associated with (poly)phenols are due to antioxidant mechanisms. However, we now know that these compounds are extensively metabolised *in vivo* yielding metabolites which are found in circulation in very low levels (nM- μ M) and have a much lower antioxidant capacity, hence this is highly unlikely. So much so after the USDA (United States Department of Agriculture) has removed their antioxidant database (ORAC Database) from its website acknowledging that the data cannot always be extrapolated to human health.

A definitive mechanism driving (poly)phenols' vascular effects is still yet to be proven, however, we have recently confirmed that it is the metabolites (rather than the native compounds) that play a crucial role in mediating vascular function³. One potential mechanism is that they increase circulating nitric oxide. Despite the structural differences, different (poly)phenol classes yield many similar metabolites, an example of this is the production of ferulic acid and associated sulphates and glucuronides. Ferulic acid is structurally very similar to apocynin (an established NADPH-oxidase inhibitor), hence it is quite possible that (poly)phenols may act in a similar way, inhibiting NADPH oxidase and hence formation of reactive oxygen species, thus increasing nitric oxide bioavailability.

Dietary approaches to managing cardiovascular disease are becoming accepted by both

patients and medical professionals, but a better understanding of the benefits of different food components is essential. (Poly)phenol rich foods offer promise for the treatment and prevention of cardiovascular disease.

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Figure 1: (Poly)phenol classification

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Cinderella called MR: Low dose spironolactone as therapeutic target against cardiometabolic disorder induced by estrogen deficiency

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Globally, cardiometabolic disorder is assuming an increasing role as a major cause of morbidity and mortality. Cardiometabolic disorder identifies a cluster of metabolic disorders that occur together; affected individuals have up to 2 times higher risk of a major cardiovascular event, 3 times higher risk of chronic renal insufficiency, more than 4 times higher danger of developing type 2 diabetes mellitus, incidence of congestive heart failure and cardiovascular mortality. Sex differences seem to

have a say in the development of cardiometabolic disorder; a women's risk increases sharply during menopause, a state of estrogen deficiency. The fact is this: many women will spend the second half of their lives in a state of estrogen deficiency. Thus, the contribution of estrogen deficiency in the pathobiology of multiple chronic diseases in women is a conceivable therapeutic challenge of the 21st century and worth looking into. This made me have a keen interest in this aspect of science as