Flavonoid content of some Australian grown apples and potential health implications

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Consumption of high-flavonoid apples may provide benefits on heart health. The newly cultivated BRAVO™ apple has one of the highest flavonoid contents of all varieties tested.

Why breed a new apple for heart health?

Cardiovascular disease refers to all diseases and conditions involving the heart and blood vessels. It is the leading cause of death, both in Australia and worldwide. According to the Australian Bureau of Statistics, on average one Australian dies every 12 minutes as a result of cardiovascular disease. Despite substantial improvements that have been seen in the past four decades, it still remains a large burden on our economy. Many more cases of cardiovascular disease can be prevented by simple changes to our diet and lifestyle. In fact, one of the most consistent relationships observed in large population studies is that a diet high in fruit is associated with a lower risk of cardiovascular disease [1-4]. When the results of 16 population studies were combined, the risk of dying from cardiovascular disease decreased by 5% for each additional serving of fruit per day [5]. Another study has shown that a diet low in fruit is one of the greatest contributors to total mortality worldwide, third only to high blood pressure and smoking [6]. Higher apple intakes are associated with a lower risk of coronary heart disease and stroke [7]. Apples, the second highest consumed fruit due to widespread geographical and seasonal availability, are an important contributor to the intake of dietary components linked with cardiovascular disease prevention. Apples have been shown to have beneficial effects on blood vessel function and blood pressure [8], cholesterol levels [9], inflammation [10] and diabetes [11].

enquiries to http://www.bravoapples.com.au/ and http://fruitwest.com.au/

What is in apples that make them so good for our heart health?

Apples are made up of predominantly water (85%) and carbohydrates (14%), including fibre and sugar (primarily fructose) [12]. Apples contain vitamins (in particular vitamin C and vitamin E), and minerals such as calcium, iron, magnesium, phosphorous, potassium and zinc. Apples are also a rich source of flavonoids. Flavonoids are plant compounds that are found in almost all fruits and vegetables. Apples and other flavonoid-rich foods are a major research focus due to population studies showing a relationship between high flavonoid intake and low incidence of cardiovascular disease [13-15]. Most apple varieties are rich in the flavonoids quercetin, (-)-epicatechin, phloridzin, and anthocyanins as well as the phenolic compound, chlorogenic acid [16]. The flavonoids are concentrated in the apple skin (anthocyanins are responsible for the red colour of particular varieties) while chlorogenic acid is found in both the skin and the flesh [17]. The composition of the BRAVO™ apple is shown in the table below.

Phytochemicals and macronutrient composition of BRAVO™ apple

Flavonoids/Polyphenols	Amount in 100g	Vitamins	Amount in 100g
Quercetin (mg)	16.17	Vitamin C (mg)	<1.0
Epicatechin (mg)	0.95	Beta-Carotene (ug)	43
Phloridzin (mg)	0.7	Vitamin E (mg)	0.3
Anthocyanins (mg)	3.54	Vitamin K1 (ug)	<1.0
Chlorogenic acid (mg)	14.87		
Energy & macronutrients		**Elements**	
Total sugars (g)	13	Calcium (mg)	3.7
Total fat (g)	<0.2	Iron (mg)	0.31
Protein (g)	0.3	Magnesium (mg)	5.5
Carbohydrates (g)	15	Phosphorous (mg)	8.3
Energy (kj)	270	Potassium (mg)	130
Fibre, total dietary (g)	1.5	Zinc (ug)	74

The main components of apples thought to be protective against cardiovascular disease are flavonoids and fibre

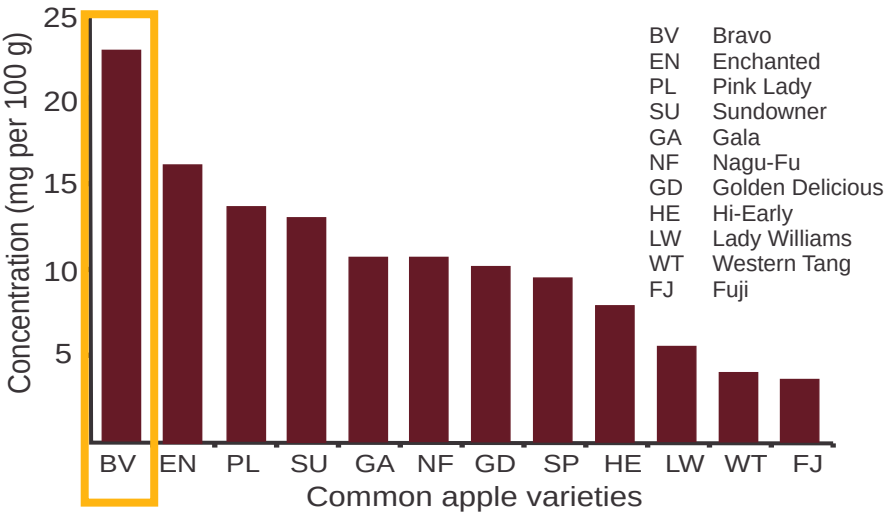
Fibre

Apples contain approximately 2.2g/100g total fibre. Of that, 70% is insoluble fibre and 30% is soluble fibre, mainly pectin [18]. Pectins are complex polysaccharides present in the cell wall of higher plants, which are not broken down in the stomach humans [19]. Beneficial health effects of pectin are attributed to it's ability to lower cholesterol [20], slow down glucose absorption [21] and it's positive effects on gut health [22] providing a food source for gut bacteria.

Flavonoids

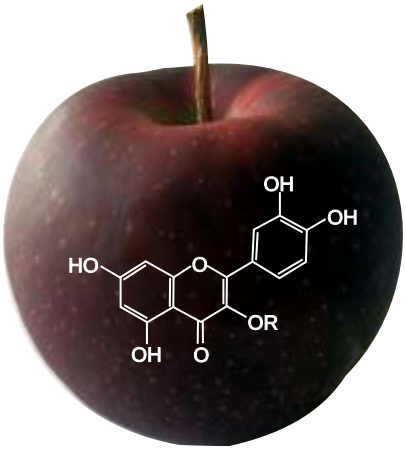
Apple skin contains considerably more flavonoids than the flesh. This is attributed to the defensive role of the skin in protecting the fruit from harmful UV light and invading pathogens [23]. The quantities of flavonoids differ substantially between varieties and are affected by geographic region, growing season and storage. The flavonoids typically found in apple skin are epicatechin, phloridzin, quercetin, and anthocyanins [24]. These compounds are found in much lower concentrations in apple flesh. Interestingly, quercetin is found almost exclusively in the apple skin. There is a significant increase in quercetin content in the skin of apples exposed to sunlight, but the levels of catechins, anthocyanins, chlorogenic acid and phloridzin are largely independent of light exposure [25]. The BRAVO™ apple is one of the most flavonoid-rich apples grown in Western Australia (see graph below). It has a high level of anthocyanins in its skin, giving it a dark red colour.

Total flavonoids in Australian apples



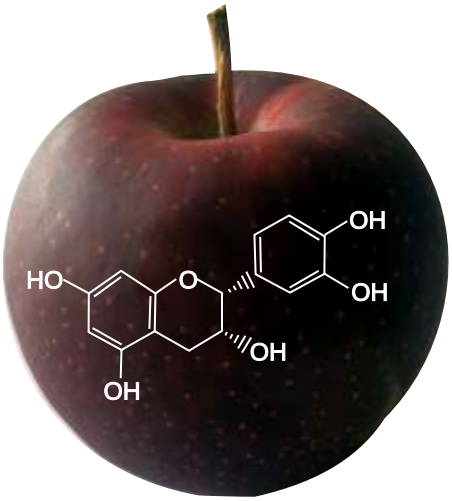
Quercetin

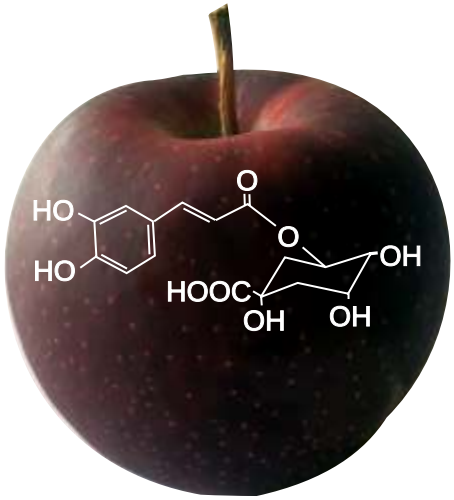
Quercetin is found almost exclusively in the skin of apples. Quercetin is also found in other foods including onions, curly kale, leeks, broccoli and tea [26]. The way in which our bodies absorb quercetin depends on the form in which it is ingested. Although you can buy quercetin in capsules over the counter, the form in which quercetin is found in whole foods (such as apples) is much better absorbed in the body [27]. There is evidence that quercetin can improve blood vessel function, lower blood pressure, act as an antioxidant and reduce atherosclerosis, the process of damage to the arteries that is the main cause of heart disease [28].



Epicatechin

Although epicatechin is found in apple flesh, it's concentration is much higher in apple skin. Epicatechin is also found in foods such as chocolate, fruits, berries and nuts. Epicatechin rich foods have been shown to improve blood vessel function, reduce blood pressure, reduce cholesterol absorption, improve cognitive function and be associated with lower risk of diabetes. Higher intakes of foods rich in epicatechin have also been linked with lower levels of heart disease [30].



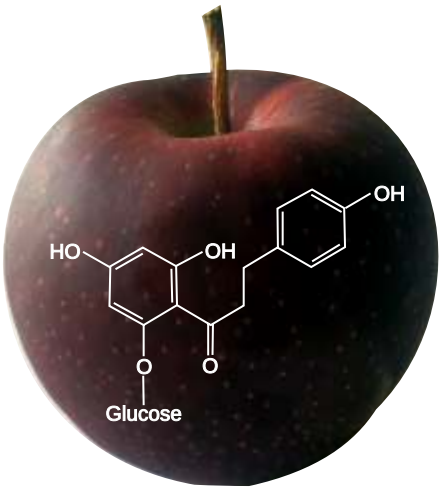


Chlorogenic acid

Chlorogenic acid is found in both the flesh and the skin of apples. It is also found in foods such as coffee, sunflower seeds and blueberries. It is proposed that chlorogenic acid plays a key role in regulating how our bodies metabolise both sugar and fat. The wide range of potential health benefits of chlorogenic acid include potential anti-diabetic, anti-cancer, anti-inflammatory and anti-obesity impacts although further studies are needed to confirm these effects. Additionally, studies have shown that high chlorogenic acid consumption is linked with lower levels of heart disease, diabetes, cancer and obesity [29].

Anthocyanins

Anthocyanins are found in apples and contribute to the redness of the skin. Anthocyanins have been shown to reduce cholesterol and blood sugar levels. They are also linked with lower levels of coronary heart disease, lower blood pressure and reduced blood vessel stiffness [31].



Phloridzin

Apples are unique for their high phloridzin content. Although evidence for health benefits of phloridzin is limited, the main health benefits described for phloridzin are it's ability to lower blood sugar concentrations and promote weight loss, suggesting it may play a role in preventing the development of diabetes [32].

Why we need both fibre and flavonoids

There are a large number of flavonoid supplements on the market. However, these are lacking the fibre that is found in whole foods, such as apples. Ingesting both flavonoids and fibre together changes the way in which our bodies breakdown and absorb the flavonoid compounds. It has been shown that the simultaneous ingestion of flavonoids and fibre improves the absorption of the flavonoids [33] and provides more of a benefit on cardiovascular disease risk factors than administration of either flavonoids or fibre alone [20,34]. The co-ingestion of flavonoids with fibre may decrease their absorption in the small intestine, but increase the quantity that reaches the large intestine. Here the flavonoids can be broken down to compounds called "phenolic acids" and both the fibre and the flavonoids can improve gut health. This is mainly through the effect that they have on the bacteria living there. Flavonoids and fibre have both been shown to increase the quantity of beneficial bacteria and decrease the quantity of harmful bacteria, residing in our gut [35].

Scientific evidence for the beneficial effect of apples

Population studies

That a diet rich in fruit is protective against cardiovascular disease is one of the most consistent relationships observed in observational lifestyle studies [3]. In these studies data on health and lifestyle from a large population are analysed for patterns and trends. In a large cohort an association between apple intake in particular, and reduced levels of cardiovascular disease-related mortality has been shown [36]. In this study, the group of people eating the most apples had a 23% lower risk of dying from cardiovascular disease than the group of people eating the least amount of apples. It has also been shown that higher apple intake is associated with lower risk of death from any cause as well as death from cancer [37]. This is thought to be due to the high flavonoid content of apples, as a diet high in flavonoid-rich foods has also been linked to reduced levels of cardiovascular disease-related mortality [38]. In the Finnish Mobile Clinic Health Examination Survey, persons whose diet was rich in the flavonoid quercetin were less likely to die from coronary heart disease (damage or disease in the heart's major blood vessels) [13]. In this study apples and onions were the main sources of quercetin. Additionally, in this study apple intake was associated with lower occurrences of both type-2 diabetes and stroke. Fibre has been shown to lower the risk of cardiovascular disease and, as discussed above, may be another component of apples contributing to positive effects on health. When the results of 22 population studies were combined, a 4g/day increase in fibre from fruit was associated with an 8% reduction of coronary heart disease.

Effects on blood pressure and blood vessel function

High blood pressure, an important risk factor for cardiovascular disease, is a key outcome in many studies investigating the benefits of flavonoid-rich foods on cardiovascular health. Additionally, an impairment in blood vessel function can have large impact on blood pressure and can lead to the development of diseases such as atherosclerosis (the build-up of fats, cholesterol and other substances in and on the blood vessel walls) and stroke (damage to the brain from interruption of its blood supply). One study has shown a decrease in blood pressure after apple consumption [8]. As mentioned above, flavonoids are found in much higher concentrations in apple skin compared to apple flesh. Interestingly, in this study, the lowering of blood pressure was only seen when apple was given with its skin (which has a very high concentration of flavonoids) and no effect was seen when apple flesh (which has a low concentration of flavonoids) was given. As well as lowering blood pressure, high-flavonoid apples (whole apples) have been shown to improve blood vessel function while low-flavonoid apples (apple flesh only) had no effect. Although the positive effects of apple consumption on blood vessel function have been attributed to flavonoids, it is possible that the outcome may have been influenced by an increase in fibre intake. According to the USDA National Nutrient Database, apples with and without skin have 2.4g and 1.3g fibre per 100g, respectively. In fact, an improvement in blood vessel function has been shown after a high fibre meal [39], possibly due to products produced by the breakdown of fibre in the colon [40].

Effects on cholesterol

High cholesterol is a risk factor for cardiovascular disease. It can limit blood flow, increasing the risk of a heart attack or stroke. The potential for apples to reduce cholesterol levels has been investigated in several clinical trials. The combined results of nine clinical trials showed that the daily intake of approximately 3 apples resulted in a 5-8% decrease in total cholesterol [9]. The consumption of refined apple juice may have a negative effect on plasma cholesterol levels possibly due to its high sugar and low fibre content [41]. In another study, significantly lower levels of cholesterol were found after 6 months of dried apple consumption in comparison to 6 months of dried plum [42]. Initially fibre was considered to be the key cholesterol-lowering component of apples as apple fibre (pectin) has been shown to decrease plasma cholesterol in humans [43]. Although the cholesterol lowering effect of pectin is well reported [44], the relatively low pectin content of apples suggests that there are other components of apples, such as flavonoids, which may have an effect. In humans, 4 weeks supplementation of 1500 mg apple flavonoids (a very high dose not achievable with diet) decreased total cholesterol by 4.5% in 48 men and women with high cholesterol [45]. Whether the same effects could be replicated with isolated flavonoid compounds was investigated in several human intervention studies. Overall, most human studies giving pure flavonoid supplements have not reported any significant changes in levels of plasma cholesterol [28, 46]. The present theory is that the cholesterol-lowering property of apples is due to an interaction between pectin and flavonoids, as they are more effective together than individually in reducing cholesterol [20, 34].

Antioxidants effects

Flavonoids have been shown to be excellent antioxidants (in a test tube) [47]. Consequently the health benefits of flavonoid-rich food have been previously attributed to antioxidant activity. However, we now know that this is not exactly how they work in our bodies. It has been suggested that flavonoids should now be considered as 'bioactives' rather than antioxidants [48]. Although individual apple flavonoids have a high antioxidant capacity, ingestion of large amounts of apples by humans does not appear to result in equivalent antioxidant effects [49]. It may be that apple flavonoids increase the production of protective enzymes [50], but further studies are required to confirm this new theory.

Anti-inflammatory effects

Inflammation underlies a large variety of human diseases and there is evidence that flavonoids have anti-inflammatory effects [51]. In a large population study of 8335 US adults, a high intake of apples was associated with lower levels of C-reactive protein (CRP), a biomarker of chronic inflammation [10]. Apple flavonoids demonstrate anti-inflammatory activities, possibly by inhibiting the expression of pro-inflammatory genes [52]. Another important component of apples which may be, at least partially, responsible for its anti-inflammatory effect is fibre. In a meta-analysis of human intervention trials with increased consumption of dietary fibre, 6 out of 7 studies reported a significant decrease in CRP levels, a biomarker of systemic inflammation [53]. This may be due to effects on the health of the gut, which plays a critical role in chronic inflammation [54]. Whether the anti-inflammatory effects of apples are attributable to flavonoids, fibre, or a synergistic interaction between them is yet to be confirmed.

Effects on diabetes

Type 2 diabetes can increase cardiovascular disease risk. Worryingly, the incidence of type 2 diabetes is growing in Australia and worldwide [55]. Diet has a large effect on diabetes risk; in particular a diet rich in fruits and vegetables is associated with a decreased risk of diabetes [56]. Specifically, apples have been highlighted as an important component of the diet that has the potential to reduce the prevalence of diabetes. In a large population study of 38,018 women, the consumption of more than one apple per day was associated with a 28% lower risk of diabetes when compared to women who consumed no apples [57]. One study has shown delays in glucose absorption after the consumption of both clear and cloudy apple juice [11]. These effects were suggested to be due to phloridzin and other apple flavonoids. Evidence for the potential role of apples in preventing diabetes comes mainly from animal and cell-culture studies. High blood sugar, a risk factor for diabetes, can be prevented through the inhibition of glucose uptake in the small

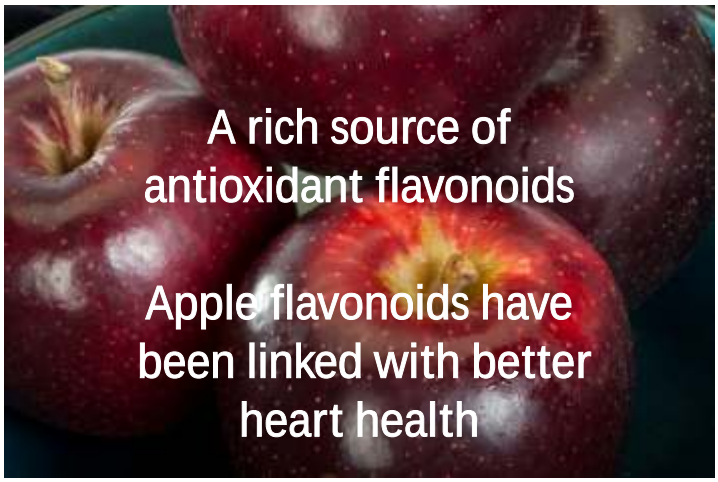
intestine. It has been shown that apple flavonoids can influence glucose uptake in the small intestine by inhibiting the activity of glucose transporters [58]. Another important apple component which may influence blood sugar levels is pectin, which can slow glucose absorption by trapping carbohydrates [59]. In a study of 12 diabetic patients, 4 week supplementation of 20 grams of apple pectin per day improved glucose tolerance [21]. In a human intervention study the apple flavonoid, epicatechin, improved plasma insulin levels (a hormone critical for regulating blood sugar levels) [46]. Several animal studies show that quercetin (found in high concentrations in apple skin) lowers blood glucose levels in diabetic mice [60]. Conclusive evidence that apples can reduce the risk of diabetes is still required, however there are indications that both apple flavonoids and pectin can reduce glucose absorption in the small intestine, preventing high blood sugar.

Effects on gut microbiota

The gut microbiota is the complex community of microorganisms that live in our digestive tract. Some human gut microorganisms are beneficial as they ferment dietary fibre into compounds called short-chain fatty acids (SCFAs), which have positive effects on our health. Other microorganisms can be harmful and have been linked with inflammation and obesity. Our diet has a large influence on the microorganisms living in our gut. It appears as though the interaction between flavonoid-rich foods and the gut microbiota is reciprocal; the microorganisms in the large intestine can release the flavonoids from the fibre matrix and break them down into smaller compounds called phenolic acids while the flavonoids stimulate the growth of beneficial bacterial species and inhibit the growth of harmful species [61]. Apple pomace has been shown to have beneficial effects on rat gut health, both by increasing SCFA production and modifying the environment of the gut in such a way that supports the growth of beneficial microflora and inhibits the growth of harmful microorganisms [62]. Additionally, quercetin supplementation has been shown to inhibit the growth bacterial species associated with obesity [63]. Interestingly, the co-ingestion of apple pectin with a flavonoid-rich apple concentrate resulted in more effective gut fermentation than separate ingestion, signifying a synergistic effect of fibre and flavonoids in apple [20].

Conclusions and future research

Population studies have shown that higher apple intake is associated with a lower risk of death from any cause, cardiovascular disease, stroke, cancer and diabetes. Human clinical trials have shown some beneficial effects of apples on risk factors for cardiovascular disease such as blood pressure, blood vessel function, cholesterol and inflammation. Individual compounds which may be "responsible" for the positive effects of apple on our health, in particular flavonoids, are a major research focus. But is it really one isolated compound or is it the unique combination of flavonoids, fibre and perhaps other components in whole foods that is beneficial? There is evidence of a synergistic relationship between the fibre and flavonoids found in a whole apple, which is likely due to the gut microbiota. Results from these studies could provide further incentive to breed apples for elite levels of flavonoid content, in both skin and flesh. The BRAVO™ apple has the highest level of flavonoids of all varieties available in Western Australia. Promoting the consumption of this apple may be a simple and economic way of making a positive contribution to heart health in Australia.



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