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Strawberry and cranberry polyphenols improve insulin sensitivity in insulin-resistant, non-diabetic adults: a parallel, double-blind, controlled and randomised clinical trial

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Abstract

Plant-derived foods rich in polyphenols are associated with several cardiometabolic health benefits, such as reduced postprandial hyperglycaemia. However, their impact on whole-body insulin sensitivity using the hyperinsulinaemic-euglycaemic clamp technique remains under-studied. We aimed to determine the effects of strawberry and cranberry polyphenols (SCP) on insulin sensitivity, glucose tolerance, insulin secretion, lipid profile, inflammation and oxidative stress markers in free-living insulin-resistant overweight or obese human subjects (n 41) in a parallel, double-blind, controlled and randomised clinical trial. The experimental group consumed an SCP beverage (333 mg SCP) daily for 6 weeks, whereas the Control group received a flavour-matched Control beverage that contained 0 mg SCP. At the beginning and at the end of the experimental period, insulin sensitivity was assessed by a hyperinsulinaemic-euglycaemic clamp, and glucose tolerance and insulin secretion by a 2-h oral glucose tolerance test (OGTT). Insulin sensitivity increased in the SCP group as compared with the Control group (+0·9 (SEM 0·5) × 10^{-3} *v.* −0·5 (SEM 0·5) × 10^{-3} mg/kg per min per pmol, respectively, $P = 0{\cdot}03$). Compared with the Control group, the SCP group had a lower first-phase insulin secretion response as measured by C-peptide levels during the first 30 min of the OGTT ($P = 0{\cdot}002$). No differences were detected between the two groups for lipids and markers of inflammation and oxidative stress. A 6-week dietary intervention with 333 mg of polyphenols from strawberries and cranberries improved insulin sensitivity in overweight and obese non-diabetic, insulin-resistant human subjects but was not effective in improving other cardiometabolic risk factors.

Key words: Polyphenols: Strawberries: Cranberries: Insulin sensitivity: Glucose metabolism: Insulin secretion: Insulin-resistant subjects

According to the International Diabetes Federation[1], up to 592 million people worldwide (one in ten adults) will suffer from type 2 diabetes by the year 2035. This alarming increase has been predicted based on several factors, such as the high prevalence of obesity and sedentary lifestyles[2,3]. Indeed in obese humans, elevated levels of NEFA, pro-inflammatory cytokines and other factors produced by adipose tissue are key determinants of insulin resistance[4]. To maintain plasma glucose at normal levels, pancreatic β-cells must adjust their function to compensate for insulin resistance. This leads to an exhaustion of β-cell insulin secretion and the development of impaired glucose tolerance (IGT) and subsequent type 2 diabetes.

In recent decades, scientific evidence has shown a link between increased consumption of fruits and vegetables, particularly berries, and reduced incidence of type 2 diabetes[5]. Recent reviews have indeed reported that berries, like strawberries and cranberries, can lower markers of cardiometabolic risk[6–11] and improve markers of the metabolic syndrome in humans[12–14]. It is well-documented that strawberries and cranberries are rich in polyphenols and contain a wide variety of phenolic compounds, ranging from phenolic acids (hydroxybenzoic and hydroxycinnamic acids), flavonoids (anthocyanins, flavonols and flavan-3-ols) to polymerised molecules (proanthocyanidins and ellagitannins)[15]. According to several *in vitro* and animal studies, polyphenols may improve glucose metabolism[16] and peripheral glucose uptake in insulin-sensitive tissues by increasing GLUT4 translocation and activity and reducing oxidative stress and inflammation[17,18]. It has recently been demonstrated that anthocyanin-rich bilberry

Abbreviations: IAUC, incremental AUC; IGT, impaired glucose tolerance; *M/I*, insulin sensitivity index; OGTT, oral glucose tolerance test; SCP, strawberry and cranberry polyphenols; UHPLC, ultra-high performance liquid chromatography (UHPLC).

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